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RESULTS OF ROENTGEN TREATMENT OF LEUKEMIA*

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THE value of roentgen treatment in chronic leukemias is generally acknowledged as an excellent palliative measure. There is optimism and pessimism in the varied reports of results, especially in the statistical appraisals of a possible increase in the longevity cycle.

It was for this purpose that a review of the records of all cases of chronic myelogenous and lymphogenous leukemia at the Philadelphia General Hospital was undertaken five years ago. The findings at that time were considered disappointing. The history records and pertinent laboratory data were interpreted as being confusing, and the report was accordingly set aside. Since that time additional patients and further changes of technique have been observed. The problem and the interpretation of results were considered from another point of view. All pertinent factors in the clinical status were evaluated. Special attention was directed to an estimation of the life span in relation to the many varied technical factors employed.

It was hoped that there might be strong evidence to support a conclusion of the possible decided superiority of a particular irradiation technique. The advantages or disadvantages of fractionated small or large doses confined to the spleen or enlarged lymph nodes, or generalized irradiation of the entire body—so-called teleroentgen or "spray" techniques—were meticulously tabulated according to the final results. The correlation and evaluation of such information was essentially the objective and special scope of this analysis, and a brief summary and interpretation of the evidence is herewith submitted.

A review at this time of the records of 110 patients shows very interesting and concrete data which might reasonably be considered a representative cross section of the actual results and experiences in the radiation management and treatment of chronic leukemia. This evaluation includes all cases, even the very advanced, in which no significant irradiation could be given. Practically all the cases in the series were relatively comparable. Their illness was sufficiently severe to require hospitalization. The ratio of age, sex and race showed no significant deviation from that noted in other reports in the literature.

The symptoms were strikingly insidious. They were predominantly weakness, loss of weight, cough, dyspnea, edema of extremities, abdominal pain and fullness. Enlargement of the spleen and lymph nodes varied in degree but was usually marked and generalized.

* From the Department of Radiology of the Philadelphia General Hospital. Read at the Joint Meeting of the American Roentgen Ray Society and the Radiological Society of North America, Chicago, Ill., Sept. 24–29, 1944.

Biopsies of bone marrow (sternal) and lymph nodes were done in 21 per cent of the cases.

Of the 110 patients, 46 were too ill to undergo treatment (Table 1). They were practically moribund when admitted to the hospital. Two of these cases were clinically acute myeloid and 2 cases were acute myeloid-aleukemic types. None lived longer than one month. It is interesting to note that almost all of these patients had been ill less than six months before hospitalization. In 7 cases the duration of symptoms was less than two weeks, yet the subsequent clinical course showed them to be chronic cases. In 6 instances the symptoms had been present longer than one year.

TABLE I

	Number of Cases		
	Lymphoid	Myeloid	Total
Too advanced for irradiation	25	21	46
Irradiation: no "follow-up"	9	6	15
Irradiation: Adequate "follow-up"	24	25	49
	58	52	110

Of the patients to whom irradiation was administered, 15 could not be traced after discharge from the hospital. This group obviously cannot be considered for any statistical purpose.

The present study is limited to 49 patients who were followed throughout their illness. Of these, 28 died, and 21 are still under active treatment (Chart 1). Twelve patients (50 per cent) lived six months or less; 17, or 70 per cent, lived three years or more; 7 lived more than five years. Two patients lived thirteen years, 1 eighteen years and 1 nineteen years. This is a good summary of the status of the controlled irradiated patients in relation to the life span from the time of diagnosis and the

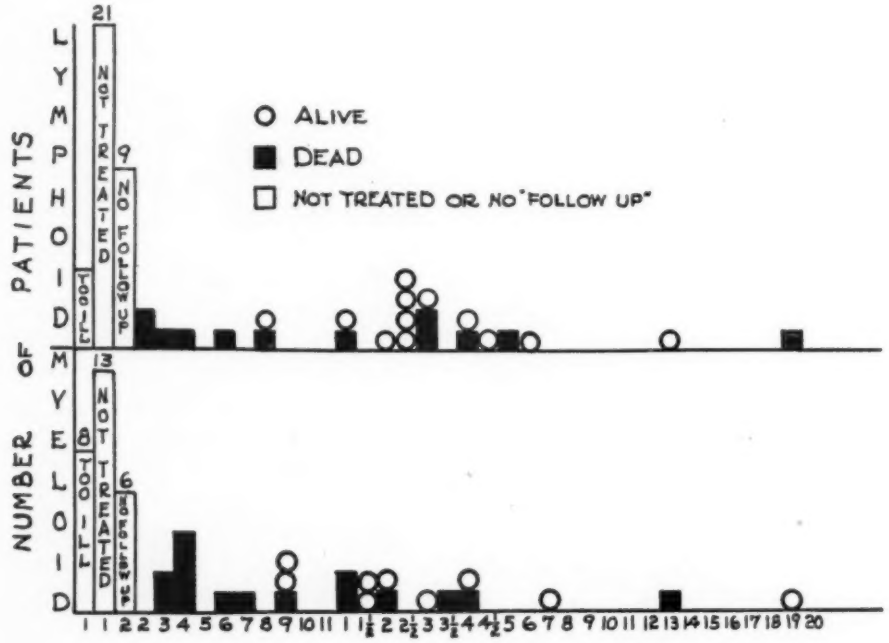

CHART 1. The life span from the time of instituting treatment is shown. About 40 per cent of the patients were too ill for irradiation when admitted to the hospital. Of the irradiated patients 13 per cent could not be traced. The life span after instituting treatment was 39.7 months for the lymphoid, and 32.2 months for the myeloid leukemias.

beginning of treatment. There was practically no appreciable difference in the clinical course or the life span of the lymphoid and myeloid types.

It might be argued that the ones who died within six months were too advanced in their disease when treatment was started. Obviously not all of the patients could be identical in extent of clinical involvement except insofar as they required hospitalization.

ment was 39.7 months (3.3 years), in the myelogenous group 32.2 months (2.7 years). One could easily add a year or more to these results if the life cycle were to be estimated from the patients' statements as to the onset of the disease. But such a method of estimating the life span for a large group would lead to erroneous conclusions, and it would undoubtedly be misleading to accept the results of such calculations.

There were 2 patients in each group

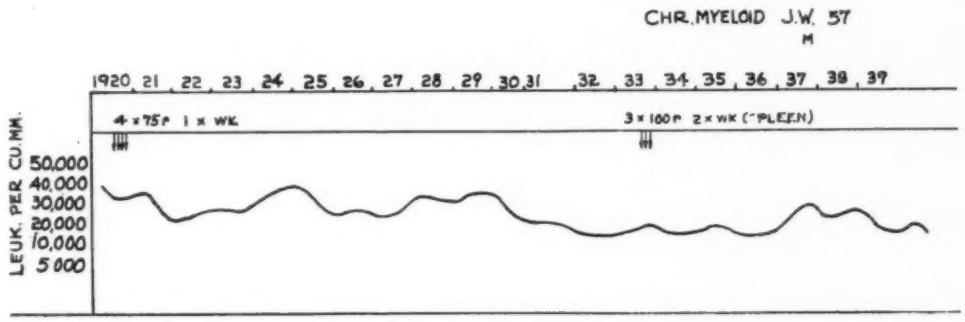

Chart II

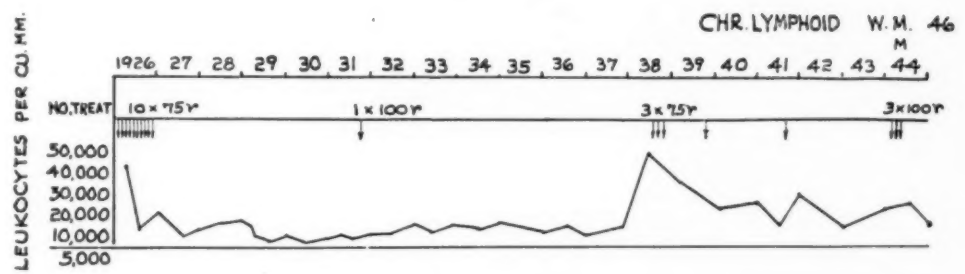

Chart III

Charts II and III. Long life spans and excellent clinical courses may be due to a benign character of the disease rather than to the effect of irradiation. Small fragmentary doses may have been contributory.

The difference in results must therefore be attributed to some inherent difference in the origin, character and extent of the disease, as well as to age and various complications. The factors of sensitivity and resistance to irradiation are variable.

If one were to evaluate the results of irradiation on the basis of duration of life in this group of 49 patients, the good effects would be undoubted and striking. In the lymphogenous group, the average duration of life from the time of instituting treat-

(Chart 1) with life spans extending to thirteen and eighteen years in the lymphoid, and thirteen and nineteen years in the myeloid group. Unless one could show a consistent uniformity of long life for a large number of patients, it would be incorrect, for statistical purposes, to accept a mathematical determination of results in terms of life span, but rather a conclusion of value based on clinical observations.

The 4 instances in this series of an unusually long life may be the effect of a very

benign character of the disease and not attributable directly to irradiation (Charts II and III).

These results show that 30 per cent of all patients irradiated may live three years or more. About 40 per cent will be too ill to tolerate enough treatment to be of benefit. Of the treated cases, more than 50 per cent will show clinical improvement which may be of a very dramatic degree. Actual prolongation of life, which is undoubted in some patients but questionable or indeterminate in others, cannot be mathematically established for statistical purposes.

According to Minot, Buckman and Isaacs[1] (1924), the average duration of life of 78 irradiated patients with chronic myelogenous leukemia was 3.5 years after detection of the first symptoms, as compared with three years for the non-irradiated patients. Minot and Isaacs[2] did not believe irradiation prolonged life in cases of chronic lymphatic leukemia.

Hoffman and Craver[3] reported the aver-

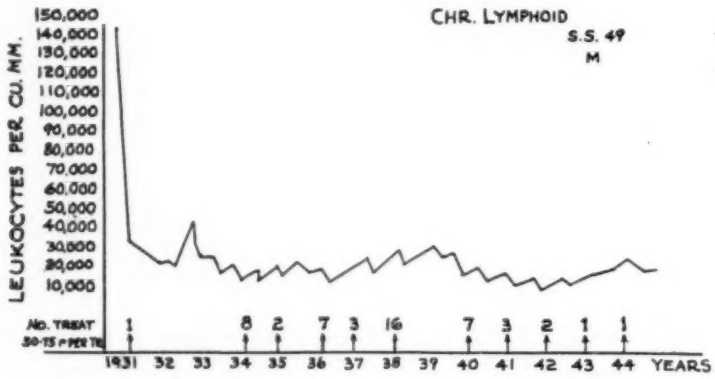

CHART IV

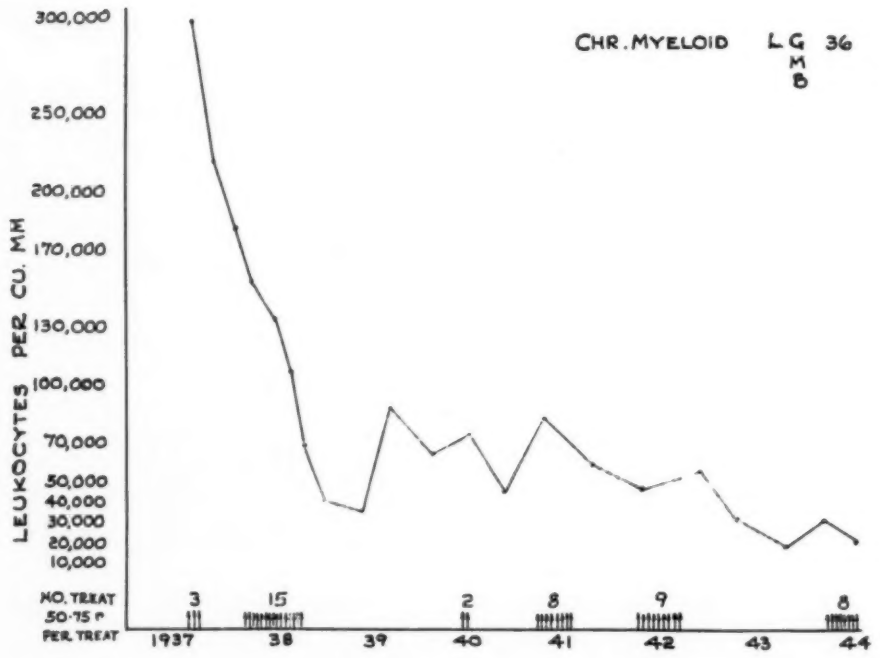

CHART V

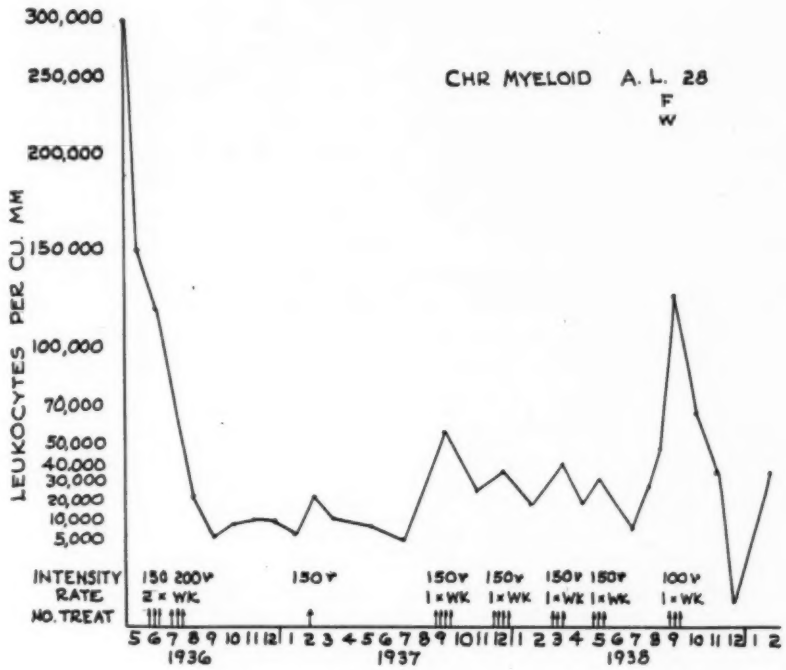

Chart VI

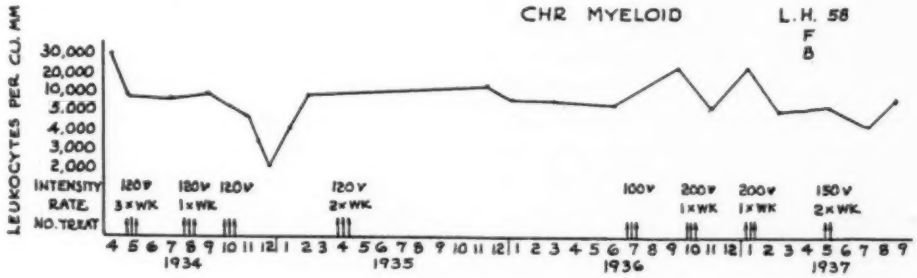

Chart VII

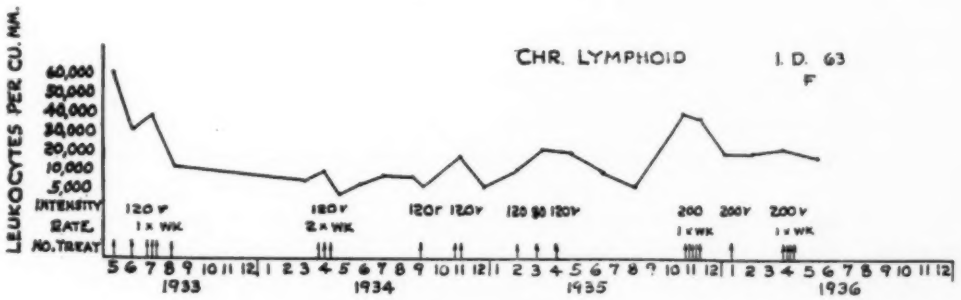

Chart VIII

Charts IV, V, VI, VII and VIII. Typical course of the leukocyte count with a manifold variety of small and large doses given at long, irregular intervals.

age duration of life after beginning treatment was 2.62 years for 82 patients with chronic myelogenous leukemia. They comment that "irradiation treatment causes an average increase of about ten months in the duration of efficient life as well as a period of efficiency and usefulness that the patient otherwise could not hope to enjoy."

The diverse clinical, pathological and technical factors make it very difficult to estimate for statistical purposes the life cycle of these patients from the onset of symptoms. No matter how painstakingly the histories may have been recorded, the first symptom as reported by the patient is not always reliable evidence of the onset of the disease. In many individuals the diagnosis has been made accidentally in routine blood studies. In this review, one patient was being prepared for tonsillectomy and another was admitted with pneumonia when the diagnosis of leukemia was made.

The history record of the first symptom and the time of onset may have no relation to leukemia. In this report, this information was not clearly or definitely recorded, and in many of the history charts the evidence was vague or contradictory. The occasional record of symptoms of long duration (three or more years) could easily raise the averages of the life span and the conclusions would therefore be misleading.

Each patient is an individual involving special details in treatment and in interpretation of the results. Patients with very mild or so-called benign types of leukemia may carry on for years with little or no irradiation. Patients with the fulminating or so-called malignant types, with very marked lymph node or splenic enlargement and rapidly failing health and strength, usually show progressive involvement unless treatment is instituted.

The blood count is a reliable criterion of the progress of the disease. Treatment should be withheld until the patient's symptoms require alleviation. In this series, many patients maintained an excellent status of well being and apparent good health with leukocyte counts ranging from 50,000 to 100,000. Under these circumstances, no irradiation was given unless there was evidence of general indisposition, pain (predominantly in the region of the spine or joints), or marked lymph node or splenic enlargement.

Iu many instances it is necessary to continue roentgen treatment until the leukocyte count reaches 40,000 or 50,000. There may be some risk in aiming to maintain a normal leukocyte level. A progressive reduction to a dangerously low level may occur even after treatment has been discontinued.

Many individuals show a marked tolerance for a very high leukocyte count and, conversely, many will manifest alarming symptoms with a relatively low, almost normal blood picture.

The use of the basal metabolic rate to indicate and to support the clinical manifestations of relapses is very excellent, as recently observed by Uhlmann and Goldner[4] and previously described by others.[5,6] It was employed in a small number of cases in this series. The high rate was not always commensurate with the sense of well being. It probably indicates distinct evidence of activity and is possibly a criterion for the need of irradiation despite the blood findings, which do not always reflect the actual condition of the patient. This evidence of a relapse or renewed activity is usually manifested readily and sometimes unmistakably in the general clinical course and well being of the patient.

The complexities of repeated relapses during the period of observation and treatment vary in frequency and intensity, and occur regardless of the technical procedures employed. In Murphy's[7] series of cases this problem seemed to be controlled when he employed the "spray" technique as against a kind of intermittent massive dose technique. There was also an improvement in the life span of patients so treated. Murphy regulates the frequency of treatments according to the blood picture, which he aims to keep below the level of 30,000 to 40,000. In this series the number of patients

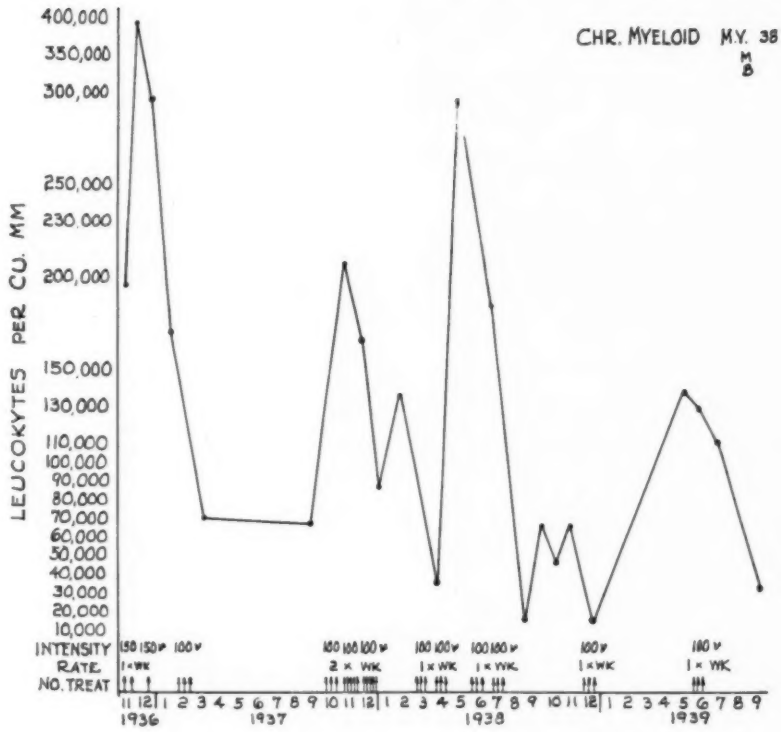

Chart IX

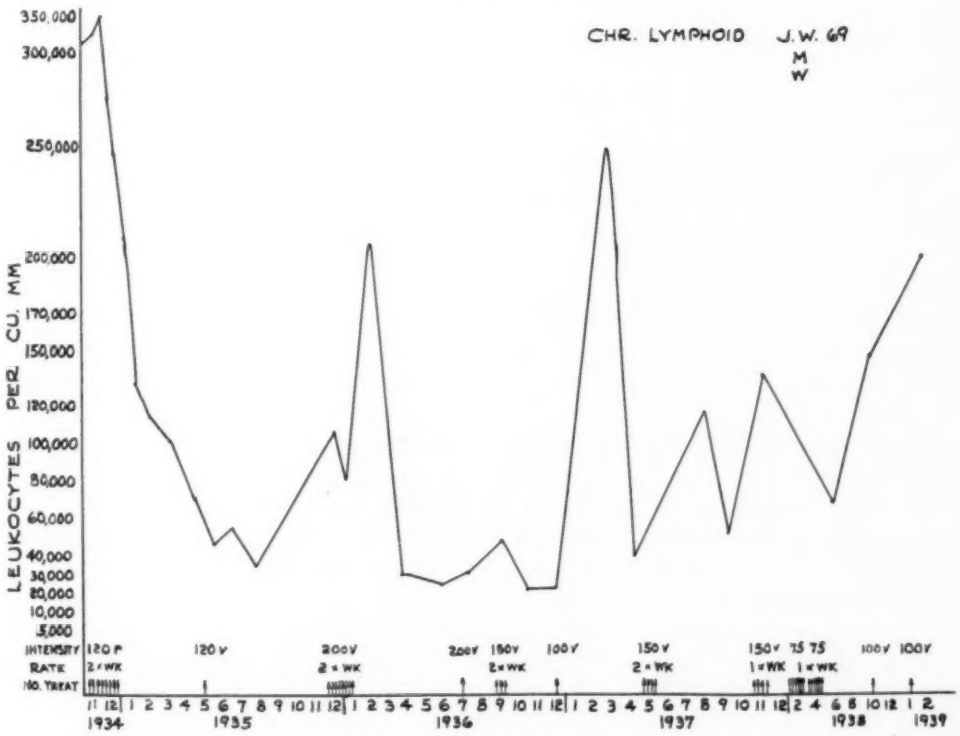

Chart X

Charts IX and X. Excellent clinical course even though the leukocyte count is high and relapses frequent. Note the long intervals between the treatments. Illustrates the variability of technique and leukocyte course in many favorable cases in this series.

treated with a teleroentgen technique was small. The results were not essentially different from those obtained with other localized, fractionated small and large doses.

In reviewing the literature one is impressed with the many variations of technique with reference to intensity, rate of delivery, size of field, and region treated. Excellent results, with life spans of four and five years and sometimes longer, have

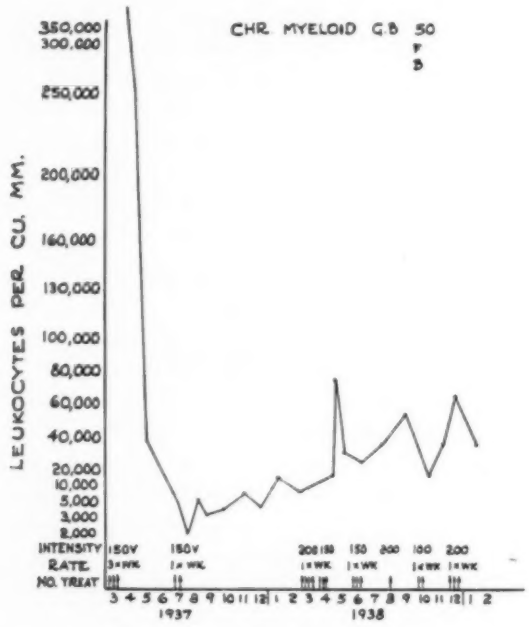

Chart xi. Favorable course with no treatment for one year, also illustrated in Charts v, vii and xiv.

been shown with a manifold variety of techniques. As in this series, no standard procedure of daily or total dose was uniformly satisfactory (Charts iii, iv, v, vi, vii and viii).

A high level in the leukocyte count may be reduced rapidly to levels of 8,000 to 10,000 and consistently maintained with a commensurate well being of the patient (Charts vi, xi, and xiv). Such a vigorous, intensive procedure in as many more patients would result in disaster—shock, collapse and shortened life. In this series of cases, the clinical course of a large group of patients was as satisfactory with leukocyte counts approximating 100,000 (Charts ix and x) as was noted in groups purposely maintained at levels of 50,000 and 25,000 (Charts vii, viii, xi, xii and xiii).

On the other hand, there were astounding variations in the clinical course, with and without treatment. Just as many patients may react well or poorly with different technical procedures of irradiation, a certain group will carry on without any kind of treatment.

There was no uniformly satisfactory technique. One should adhere to the principle of finding the smallest dose compatible with establishing a state of improvement in health and well being and efficiency. Usually 50 r (measured in air) is a safe starting basis. This may need to be given one, two, three, four or five times a week. In some cases this dose may be satisfactory if given only once or twice a month. A dose of 50 r may be sufficient at intervals of several months. The general health may be excellent for six months or a year without treatment. A satisfactory clinical status may often be maintained with these various small intensities and rates with leukocyte counts of 75,000 to 100,000, while in other groups the same clinical status is achieved only by reducing the white count to 50,000, 25,000 and 10,000 levels. This observation indicates that the rate and intensity of irradiation should be modified according to the clinical course rather than according to the leukocyte level.

There are instances when greater intensities are necessary—as much as 100, 150 and 200 r. Sensitivity to the effects of roentgen rays diminishes at variable rates (Chart vi). A patient may become refractory to the effects of small doses within six months to a year, and doses up to 200 r are necessary to bring about a stabilizing effect. In addition to regulating the dose according to the well being, one must frequently also consider additional treatment for excessive enlargement of lymph nodes or spleen.

Identical results may be obtained with 125 kv. and filtrations of 2 to 6 mm. of aluminum, and 200 kv. and filtrations of 0.25, 0.50, 1 and 2 mm. of copper. The

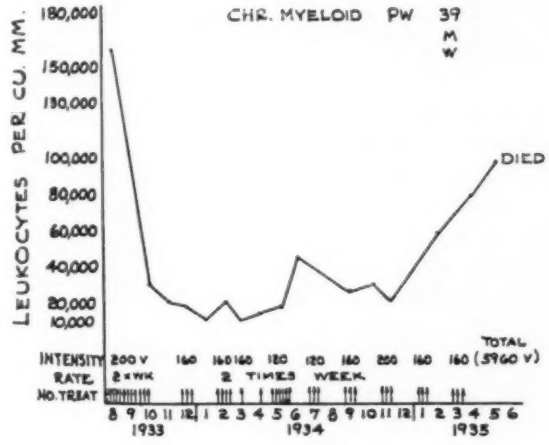

Chart xii

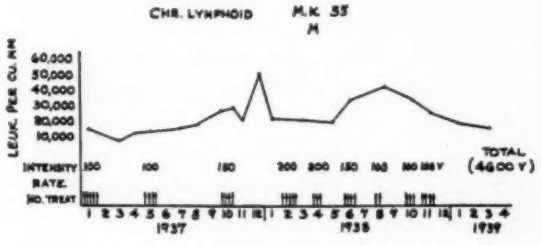

Chart xiii

Charts xii and xiii. Satisfactory clinical results accomplished with large daily and total doses and a rate of frequency that might be disastrous as a routine procedure. In an average case this would be excessive treatment.

majority of the patients were treated using fields of 15 by 15 cm. and 20 by 20 cm. over the spleen, mediastinum and ribs or over actual enlarged lymph node regions. The long bones were never specially treated except when the teleroentgen or "spray" technique was employed. A single dose of 25 r for general body irradiation was used,

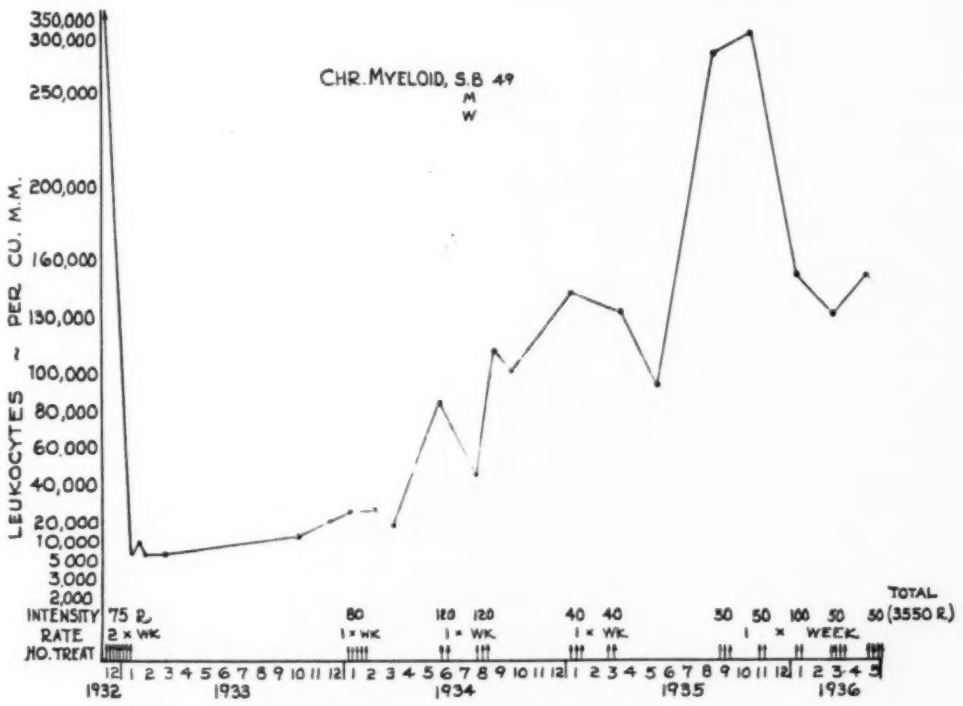

Chart xiv. Sensitivity to the effects of irradiation commonly diminishes. This is a variable factor, occurring from one to three years after institution of treatment.

but this was increased to 50 r in some cases. Localized treatment with small fields of 15 and 20 sq. cm. was generally employed and was found to be much more convenient, with results as gratifying as with irradiation to the entire body.

The variations of response to different technical factors, rate and intensity are so great that technical criteria must be determined and regulated for each patient.

In 3 cases of this series the leukocyte count dropped to 2,000, but rapid elevation occurred with relapses (Charts IV and XI). All 3 of these patients lived more than three years after these episodes. A leukopenia resulting from excessively large doses may be fatal.

The red blood cell counts varied widely in patients surviving several years or more. Fluctuations to levels as low as 2,000,000 were commonly observed. Regeneration may be expected with clinical improvement. A marked disproportion between the normal hemoglobin and red blood cell rate should be cause for alarm. This change was frequently seen in the terminal stages.

SUMMARY

Irradiation is a valuable palliative procedure. Improvement in health and strength, and very often restoration of an approximately normal efficiency, may be achieved in more than 50 per cent of patients suitable for treatment.

The life span is probably increased in a small percentage of cases, although estimations for statistical purposes may be misleading and should not be used as criteria of the value of irradiation.

The technical procedure should evolve from the smallest dose compatible with maintenance of a favorable clinical status rather than from reductions in the normal leukocyte level.*

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* For discussion see page 392.

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HEMATOLOGICAL AND CLINICAL CHARACTERISTICS OF LEUKEMIA*

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THE leukopoietic system is made up of bone marrow, lymph glands, spleen, and reticuloendothelial cells in other organs. Here arise polymorphonuclear leukocytes, lymphocytes, and monocytes. Normally the formation of white cells is a very active but orderly process, so regulated that the total number per cubic millimeter of blood varies only within narrow limits.

Under abnormal conditions, as in many infections, the number of cells released from the bone marrow is greatly increased. This increase is manifested by an accumulation of cells at the site of infection as well as by a larger number in the circulation. However, as under normal conditions, there are no very immature leukocytes. Immature cells remain in the bone marrow or at the site of formation elsewhere. The normal span of life for a polymorphonuclear cell is three to four days and for a lymphocyte about twenty-four hours. Under normal conditions five to ten billion new polymorphonuclear leukocytes and an equal number of lymphocytes, as well as many monocytes, must be released from the leukopoietic system every twenty-four hours to compensate for those destroyed.

Leukemia is fundamentally a disturbance in leukocyte formation and thus concerns primarily the bone marrow, spleen, lymph glands, and reticuloendothelial cells. It is characterized by a disorderly multiplication of cells in the leukopoietic system. Usually there is an increased number of leukocytes in the blood stream. Immature cells are almost always present, even if there is no leukocytosis. The disease suggests a neoplastic process. The blood findings only reflect a loss of normal physiologic control and balance.

All leukocytes develop extravascularly from reticulum cells through a number of intermediate stages. The primitive blood cell derived from the reticulum cell is differentiated into myeloblast, lymphoblast, or monoblast. According to the polyphyletic viewpoint of white cell formation, the line of development is already determined when this differentiation has taken place, so that one blast cell cannot change into another. Thus, a myeloblast cannot become a lymphoblast or monoblast. It can give rise only to a neutrophilic, basophilic, or eosinophilic myelocyte, which in turn becomes a mature polymorphonuclear cell. Likewise a lymphoblast becomes only a lymphocyte, and a monoblast only a monocyte. Only mature cells are released into the circulation, although new leukocytes may be less mature than normal if there is an excessive need for new cells as in lobar pneumonia.

In leukemia the cells go through these same stages, but the formation of new cells is more rapid owing to some unknown stimulation or to the loss of influences which normally control growth of the leukocyte and its release into the circulation. In acute leukemia the cells are usually very immature. The marrow is hyperplastic and often filled with immature cells, while the leukocyte count in the circulating blood may be very low. This seems to be explained by the fact that immature cells reach the circulation with difficulty even in leukemia.

Immature cells are identified by certain histological characteristics. All blast cells are without granules in the cytoplasm, which is very basophilic and so appears a deep blue with Wright's stain. Myeloblasts,

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lymphoblasts, and monoblasts are difficult to differentiate but may differ slightly in size, in number of nucleoli, and in the staining reaction of the chromatin. Often the identification of blasts depends upon the "company they keep." If the blood film shows myeloblasts and other intermediate stages of polymorphonuclear cells, the chances are that any blasts present are myeloblasts.

The chromatin in the nucleus of an immature cell is a fine interlacing thread ("lace-net"), which stains much lighter than the chromatin in the normal mature nucleus. Nucleoli are usually present. As the cells mature, the chromatin changes into heavy basic-staining material. This is the principal change in the transition of a lymphoblast into a mature lymphocyte. As a myeloblast develops, granules, which are neutrophilic, eosinophilic, or basophilic, appear in the cytoplasm to form myelocytes. Later the nucleus becomes lobulated and filamented, the chromatin takes on mature staining reactions, and thus a mature polymorphonuclear neutrophilic, eosinophilic, or basophilic leukocyte develops. A monoblast develops azure granules in the cytoplasm and changes in the nucleus to become a monocyte.

A diagnosis of leukemia is made after a hematological and clinical study. Usually the blood examination shows a leukocytosis, although a leukopenia is common, especially in acute leukemia. In a recent detailed study of 250 cases of leukemia[1] the white cell count was found to be below 6,000 per cu. mm. in 27.6 per cent, from 6,000 to 10,000 in 6.8 per cent, and over 10,000 in only 65.6 per cent. Many ill patients never have a leukocyte count above 1,000. Usually the differential count reveals immature cells. In the myeloid leukemias these may be the intermediate stages and include myelocytes, promyelocytes, and metamyelocytes, as well as myeloblasts. Immature cells may be seen in different clinical conditions, but probably a blast is seen only in leukemia.

Often in leukemia too few white cells are available for study to find many immature cells. Here concentrated preparations of leukocytes are of the greatest value. These are simply prepared by allowing the red cells to settle out by gravity for a short time, centrifuging quickly, and making films from the "buffy" coat, or layer of white cells on the surface of the red cells. In this way many white cells may be obtained for microscopic study, and blasts and immature cells are easily found. However, the cells in the circulating blood only reflect the activity of the tissues in which the leukocytes are formed. A biopsy of the bone marrow may be obtained by trephining the sternum or some other bone. In most cases, however, an entirely satisfactory specimen of the marrow may be secured by aspirating the sternal marrow with a large needle and making coverslip preparations from the aspirated material. When the diagnosis is difficult otherwise, leukemia may be disclosed by an examination of the marrow. In all doubtful cases a study of the bone marrow is mandatory.

Myeloid, lymphoid, and monocytic leukemia in which the predominant cell is of myeloid, lymphoid, or monocytic origin may occur in both acute and chronic forms. In 400 cases of leukemia seen during the past fourteen years in the hematology laboratory at the Cleveland Clinic the distribution has been as follows: (1) acute myeloid or myeloblastic, 16.5 per cent; (2) chronic myeloid, 24.7 per cent; (3) acute lymphoid or lymphoblastic, 15.3 per cent; (4) chronic lymphoid, 29.5 per cent, and (5) acute and chronic monocytic, 14 per cent. The disease is much more prevalent in men than in women. Sixty-one per cent of the 400 cases were men. Persons of every age are affected. In our series the ages varied from three and a half months to seventy-eight years.

Since lymphoid and reticuloendothelial cells are scattered throughout the body in many different tissues, the hyperplasia characteristic of leukemia affects almost all organs. Enlargement of the lymph glands, spleen, and liver is common. The

bone marrow is hyperplastic and accordingly is hypertrophied. The wide distribution of the disease is largely responsible for the widely varying clinical picture. Immature white cells may infiltrate any organ.

Toxemia is characteristic of leukemia, and certain symptoms are typical of toxemia. The more important are fever, loss of weight, sweating, anorexia, malaise, and joint symptoms. The exhaustion so common in all types of leukemia is due in part to toxemia and in part to anemia. In most cases the anemia seems to be due to overcrowding of the marrow spaces by leukopoietic overgrowth, thus preventing normal red cell formation. Toxemia by its depressing effect on the bone marrow, however, is often a factor in the anemia. Especially in acute cases the marrow may be even aplastic although immature, making the differentiation of primary aplastic anemia and leukemia most difficult. The aplasia can be explained only on the basis of the effect of toxemia on the bone marrow.

Anemia, hemorrhage, and infection are very common in leukemia. These result from the characteristic toxemia and infiltration of tissues.

Rarely does a patient have active leukemia without anemia. A hemoglobin as high as 80 per cent was found in only 24 of the 250 patients studied. Only 3 patients with acute leukemia had a normal hemoglobin. Most of the patients without anemia had chronic lymphoid leukemia. The anemia is due to a depression of bone marrow by the toxemia and an actual crowding out of red cells by the overgrowth of white cells in the marrow. The characteristic symptoms are weakness, dyspnea, and pallor.

The anemia may be of any type. Seldom, however, is a marked microcytic or hypochromic anemia encountered, unless blood loss has been severe. In many cases the anemia is definitely macrocytic, especially in the leukopenic patient, and pernicious anemia may be suspected. The macrocytosis of leukemia is not adequately explained. An increased size of red cells is looked upon as indicating a deficiency in supply or lack of use of the erythrocyte-maturing factor present in liver extract. In leukemia the supply of the specific maturing factor is evidently adequate, since the anemia is not influenced by giving more of the specific maturing principle. The disease probably interferes with utilization of the erythrocyte-maturing substance in the bone marrow. At times the anemia is hemolytic. The platelet count is very variable. This may be very high in chronic myeloid leukemia, but in acute leukemia the number of platelets is often so greatly reduced that thrombopenic bleeding occurs. The thrombopenia may be due to crowding out of the megalokaryocytes in the marrow or to depression of marrow function by toxemia.

Hemorrhage is a frequent symptom in leukemia. In about 10 per cent of the 250 patients abnormal bleeding was the most important symptom. The tendency to abnormal bleeding is due to platelet deficiency, to increased permeability of the vessels without thrombopenia, or to a combination of these two factors. Abnormal bleeding is commonly manifested as petechiae, especially in acute leukemia. Gross bleeding, such as in the brain or from the intestinal tract, is not uncommon. Cerebral hemorrhage is a frequent cause of death in chronic myeloid leukemia, in which the number of platelets is usually increased.

Infection occurs frequently in acute leukemia in which leukopenia is very common, and the number of mature polymorphonuclear cells in the blood and tissues is greatly reduced. When normal body tissues come in contact with bacteria, infection may result from a decrease in defense cells. The more common sites are gums, tonsils, and rectum. Both infection and toxemia are responsible for the fever, which is almost always present.

The clinical picture in all types of leukemia varies greatly owing to widespread involvement of almost all tissues of the body

and to the effects of toxemia. The acute leukemias run a rapid course. The white cells in the blood are very immature. Often most of the cells seen in a stained film are blasts. A detailed analysis has been made[1] of 50 patients in each of the types of leukemia, (1) acute lymphoid or lymphoblastic, (2) acute myeloid or myeloblastic, (3) chronic lymphoid, (4) chronic myeloid, and (5) monocytic.

Acute lymphoid leukemia occurs principally in children. Two-thirds of the patients in this group were under ten years of age. The disease is rare in older persons. I have been impressed with the frequency of skeletal pains in acute lymphoid leukemia. Several patients had a definite arthritis. One boy of seven had marked swelling of an ankle and intense pain in the legs. Involvement of most of the large joints confined him to bed for two months before admission. The arthritis was associated with fever and anemia. The outstanding clinical characteristics of the acute lymphoid group, however, are anemia and weakness and an abnormal tendency toward bleeding usually manifested by easy bruising. The spleen was enlarged in most of our cases. Often enlarged glands were complained of, but the enlargement was minimal. Perhaps this group conformed more closely to the textbook description than any of the other groups. When a child presents fever, anemia, easy bruising, and enlarged glands and spleen the diagnosis is usually acute lymphoid leukemia. Here again leukopenia is common, although very high counts are observed also. The anemia is usually severe. It is seldom macrocytic and often microcytic.

Acute myeloid or myeloblastic leukemia has much in common with the acute lymphoid type. The patients in this group were older, all decades from the first to the seventh being represented. Only 6 patients were under ten; the other cases were quite uniformly spread over the ten to seventy year interval. The presenting complaints were perhaps the most varied of all groups. Among these were "chills and fever," "big spleen," "swelling of the face," "stomach trouble," "sore throat," "weakness," "pernicious anemia," "muscle and joint pains," "I can't eat," and "fever." Actual joint involvement is much less common than in the acute lymphoid type. The outstanding clinical features are anemia and fever. Abnormal bleeding may be prominent but is infrequent. Infection is not so common as it is in the monocytic group. Necrosis occurs but is uncommon. The leukocyte count is seldom high. Two-thirds of this group of 50 patients had a total leukocyte count under 10,000. In 3 cases no myeloblasts could be found in the blood, although the marrow showed the typical picture of acute myeloblastic leukemia. Less than half the patients had a palpable spleen. At times there was some general glandular enlargement.

In many instances *chronic lymphoid leukemia* is mild and runs a prolonged course, although here as always the disease ends fatally. It is a disease of older persons. I have never seen this type in a young person. Eighty-eight per cent of the patients in this group were over fifty years of age; only 3 were under forty-five. Often no blast cells were seen. Usually fragile cells or smudges were present and probably represented immaturity. Even in the mild chronic cases the bone marrow showed a high proportion of lymphoid cells. The total leukocyte count was usually high. Only 1 patient in this group had a count less than 10,000. Many patients had no anemia. This is the only type of leukemia which persists for any length of time without the development of anemia.

The clinical symptoms in chronic lymphoid leukemia also are often mild. Enlargement of glands and spleen may be the only abnormality complained of by the patient for a long time. Most patients who have had leukemia for any length of time belong in the chronic lymphoid group. This type not infrequently has been an incidental finding in the examination of patients for other conditions. Patients entering the Clinic for chronic cough, iritis, abdominal pain, rheumatism, pain in the

legs, headache, leukocytosis, bladder trouble, constipation, and "sick spells" have had chronic lymphoid leukemia. In most cases the outstanding clinical feature was enlarged glands or spleen. Weakness was relatively uncommon. Infection as a complication was seldom encountered.

Chronic myeloid leukemia is characterized principally by weakness. This is partly due to anemia, which is almost always present, but the toxemia characteristic of the disease is also an important causal factor in the exhaustion. Many patients were concerned about an enlarged abdomen resulting from a marked splenomegaly. Fever is very common and was the presenting complaint in several instances. One patient was confined to a tuberculosis sanatorium for months because an acid-fast infection was suspected when the fever was really due to leukemia. The tendency to bleed is greater in the chronic myeloid than in the chronic lymphoid type, probably because of the more severe toxemia. Here the abnormal hemorrhage is not due to thrombopenia but to the toxemia effect of the disease on the endothelium of blood vessels. Usually the platelet count is high. Hemorrhage is not infrequently the cause of death. Infection is uncommon. In this group the patients' ages varied from two and a half to seventy-six years. Most patients were in the middle age group. In only 3 instances was the total leukocyte count less than 10,000. Usually the total count is high, and in over half the patients the count was above 100,000. Blasts were found in most cases.

The clinical picture of *monocytic leukemia* is more varied than that of any other group. Patients with monocytic leukemia complained most frequently of anemia or of weakness due to anemia. Anemia and weakness was the outstanding clinical feature in 19 of the 50 patients in this group. Fever alone or with anemia was also a prominent feature of the disease and was often associated with generalized body aching. Two other prominent symptoms were various types of infection and abnormal bleeding. The infection most often involves the buccal tissues, so that the diagnosis can frequently be made from the condition of the gums and other tissues of the oral cavity alone. Hypertrophy of the gums is especially characteristic and may progress very rapidly, usually with necrosis. The necrosis may become chronic and persist for months. Other patients with equally typical monocytic leukemia, as far as the hematological diagnosis is concerned, may never have infection of any kind. Abnormal bleeding may be very severe and difficult to control. It is most likely to occur in patients with evident toxemia as manifested by fever and anemia and may progress rapidly. Bleeding here is usually the result of thrombopenia.

One patient was admitted recently to the dermatological service with multiple skin ulcerations previously diagnosed and treated as furunculosis. Leukemia was not suspected until the blood examination showed 20,000 leukocytes with many monocytes and monoblasts. Sternal puncture revealed a hyperplastic marrow with a great excess of monocytes. Severe anemia was present, and the patient had a persistent fever. Biopsy of a local lesion confirmed the diagnosis of monocytic leukemia. Another patient who had only a marked anemia during the course of his disease lived several years with multiple transfusions. There was no leukocytosis, although a high proportion of the cells were monocytes. The anemia was always macrocytic. Many other equally unusual clinical histories could be detailed.

The leukocyte count in monocytic leukemia is seldom high. Sixty per cent of the patients in this group never had a count above 10,000, and only 3 patients had a count above 100,000. The anemia was macrocytic in almost one-half the cases in which the volume index was measured. The youngest patient I have seen with leukemia was three and a half months old and had the monocytic type. One-half the patients in this group were over forty-five years of age. The spleen and glands were seldom enlarged. In some cases blasts were never seen.

SUMMARY

Leukemia is a disease of the leukopoietic system characterized by the loss of normal physiologic control of leukocyte formation.

Normally there is active orderly growth of white cells in the marrow, spleen, lymph glands and reticuloendothelial system. Only mature cells reach the blood stream.

In an acute need for defense against infection and toxemia the leukopoietic tissues can supply enormous numbers of mature cells. The hyperplasia, however, is still under normal physiologic control.

Normally five to ten billion polymorphonuclear cells and an equal number of lymphocytes are supplied daily. If needed, many times this number can be supplied.

In leukemia there is a disorderly overgrowth of leukopoietic tissues suggesting a neoplastic process. This is due either to some unknown stimulation or to a loss of normal physiologic control.

Leukemia is a generalized disease and may affect any part of the body. It is characterized primarily by toxemia and cellular infiltration of organs and other body tissues.

The bone marrow is always involved. It is usually hyperplastic but may be aplastic though immature.

The typical blood finding is leukocytosis with immature cells such as myeloblasts, myelocytes, lymphoblasts, monoblasts, and intermediate cells in the circulation.

Leukocytosis is, however, often absent, especially in the acute types. In the 400 patients the leukocyte count was below 10,000 in one-third of the patients. In 100 patients with acute lymphoid or acute myeloid leukemia the count was below 10,000 in over one-half the patients.

Anemia is almost always present, and thrombopenia is common.

The signs and symptoms of leukemia are principally the result of anemia, hemorrhage, and infection due to toxemia and cellular infiltration.

The greatest variety of clinical pictures is encountered, so that little is characteristic of a patient with leukemia.

Acute lymphoid leukemia is a disease of childhood. Anemia, bleeding, and arthritis are common symptoms.

Acute myeloid leukemia occurs in all ages and presents the greatest variety of symptoms and clinical findings.

Chronic lymphoid leukemia is often a very mild disease and runs a moderate though fatal course. Enlargement of glands and spleen is the outstanding feature.

Chronic myeloid leukemia is characterized by a marked toxemia causing almost constant fever and anemia.

Oral infections with hypertrophy of the gums are prominent symptoms in *monocytic leukemia*. The spleen is seldom palpable. The leukocyte count is usually not very high. The anemia is often macrocytic.

Cleveland Clinic,
Cleveland 6, Ohio

REFERENCE

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DISCUSSION OF PAPERS BY DR. WIDMANN AND DR. HADEN

Dr. Robert S. Stone, San Francisco, Calif. It has been very interesting and instructive to listen to these papers on leukemia, since we radiologists must understand it both from the point of view of how to diagnose and treat it and from the point of view of its development in ourselves.

I was glad to hear Dr. Widmann bring out the fact that sometimes patients are overtreated and it would be better if we used smaller doses. I think that may be one thing that radiophosphorus will teach us, that it is possible to control some leukemias with smaller doses of radiation than are frequently used and that we should try to control them with the lowest possible dose.

An interesting point brought out by Dr. Haden is that one-third of the leukemic patients that he has treated did not have elevated white blood cell counts. We hear so frequently that the amount of radiation we give should be controlled by the white blood cell count. Dr. Widmann, I think, emphasized the point that we must regulate our treatment by the type of

symptom that the patient has rather than by the white blood cell count, and when you review charts such as he showed of the white blood cell count and the roentgen therapy, there may be no coördination between them at all because the treatments were given to control the symptoms and not to bring down a high white count.

I believe it is possible to cause leukemia by irradiation, and it therefore behooves us to watch more carefully the exposures that we are getting, that our technicians are getting and that industrial radiographers are getting if we wish to keep down the incidence of leukemia in those working with radiations.

Dr. U. V. Portmann, Cleveland, Ohio. It is astonishing that many radiologists have forgotten the different types of normal blood cells, the forms present in the leukemias, and the anatomic location of the principal hemocytopoietic tissues. This is one reason why Dr. Haden was asked to review this whole subject for us in twenty minutes. He has done so admirably, and I am sure we have all profited.

Dr. Widmann, in a comprehensive manner, statistically reviewed his results in the treatment of leukemias and came to the conclusion that longevity is increased by roentgen therapy but pointed out also that longevity is not the only criterion for evaluating results. We often gain the impression clinically that many patients with leukemias given roentgen therapy live longer than they might if not treated. Also economic usefulness is undoubtedly prolonged and morale improved; therefore, we should not be discouraged about the results of roentgen therapy for these incurable diseases.

Dr. Widmann also pointed out that we should not attempt to establish routine methods of treatment but should consider patients individually. In my opinion this is most important. We should take into consideration the blood picture, the condition of the bone marrow, and the general condition of each patient as indicative of when and how much treatment should be given.

Some radiologists believe that irradiation is contraindicated when the white blood cell count is less than 40,000. We have not hesitated to treat patients with what is called a leukemia, depending more upon the types of abnormal cells found in the blood than upon the number. As Dr. Haden stated, we have treated many patients with white blood cell counts of less than 10,000.

Dr. Widmann and Dr. Stone gave timely warning that the dosage of roentgen radiation given at one time should be small.

Dr. Henry J. Ullmann, Santa Barbara, Calif. There are one or two points in Dr. Widmann's paper that I wish to discuss, and with which I heartily agree. One is the question of producing irradiation sickness referred to every once in awhile in articles on leukemia. I, personally, cannot see the slightest excuse for making any patient with leukemia sick with the roentgen ray. If one does so, too much has been given.

A point that I have never heard spoken of is what I call "coasting." My method is similar to Dr. Widmann's: that is, small doses repeated as indicated by the blood count, and, if I am treating every day with, let us say, 50 r (and when I use the term r it means total skin dose, or r on the skin), a count is made each day before the treatment is given. This is important, because after a patient's blood count begins to fall, it may continue to coast downward, in some instances for several days, and if one is treating a patient with only a 10,000 to 12,000 white blood cell count, one must watch for that "coasting."

I am tremendously interested in the total polymorphonuclear count in these patients, for I treat a leukemic with very minute doses, even as low as 25 r, measured on the skin, when the count is as low as 6,000, if the total polymorphonuclear count is very low or absent, which means the immediate danger of a terminal infection. Conversely, I might not treat a patient who felt perfectly well with a count of 25,000 if there were plenty of polymorphonuclears.

At the meeting of the American Medical Association in 1940 Dr. Forkner spoke of a thrombocytopenia being produced by roentgen irradiation. I have never heard of it. I would consider such a result the sequence of gross overdosage or recklessness. The platelets usually rise as the red blood cell count rises.

Dr. W. Edward Chamberlain, Philadelphia. I just want to ask Dr. Haden to comment upon the difficulties that we have been having in differentiating between acute lymphocytic leukemia and acute leukemia of the myelogenous group. The hematologists seem to have a great deal of difficulty in this regard and we have sort of had the feeling that perhaps all

the acute leukemias would have to be grouped together with a big question mark as to how many of them are of the lymphocytic group and how many of them are of the myeloid group.

Dr. Erich M. Uhlmann, Chicago. It seems that we are all agreed that in dealing with leukemia the patients and the disease have to be treated and not the white blood cell count or any other symptom. On the other hand, laboratory tests may be of importance in timing the treatments better than it would otherwise be possible. In the past five years we have utilized the determination of the basal metabolism rate for such purposes. It is not a new discovery but it has been known for over forty years that the basal metabolism may be elevated in leukemic patients. In our material this is true in over 60 per cent of all patients treated for lymphatic or myelogenous leukemia. If the basal metabolic rate is elevated, its repeated determinations may be used as an excellent index to begin and terminate treatments. I will give you an illustration.

In 1939 a patient previously treated for lymphatic leukemia presented himself for follow-up examination. He was at that time in excellent health, had a white count of 14,000 cells, a normal differential count, no lymphadenopathy, and no other clinical signs of leukemia. A routine determination of his basal metabolism, however, revealed a rate of 69 per cent. Since the patient felt perfectly well, the possibility of an error was considered, and the test was repeated one week later. The second determination showed 71 per cent, and the patient was kept under close observation. Check-ups on the basal metabolic rate at weekly intervals showed no change, but four weeks after the first test, generalized lymphadenopathy developed, the patient grew continuously weaker, and within two more weeks the white blood cell count rose to 160,000. Following roentgen therapy instituted at that time, the basal metabolic rate dropped within three weeks to 16 per cent, the white blood cell count decreased to 120,000, but the lymphadenopathy showed little change. Roentgen therapy was then discontinued in order to observe the course of the disease. Within one month, the white blood cell count dropped to 18,000 and all clinical symptoms disappeared.

We have observed similar occurrences in about 20 patients since that time, a number of whom were reported before the Radiological Society of North America two years ago. These patients have been followed now over a five year period and of the reported group, none have died during this time. This may, of course, be only a coincidence but it might also be attributed to the fact that these patients were treated with extremely small amounts of radiation which were sufficient to control the disease and not too high to render the patients resistant to repeated roentgen treatment.

Dr. Charles L. Martin, Dallas, Texas. Will Dr. Haden be good enough to discuss the condition known as agnogenic myeloid hyperplasia? I have never made this diagnosis, but several authors have stated that it can be confused with leukemia, and that the use of roentgen therapy may be disastrous.

Dr. Haden (closing). There are two or three things to be emphasized again. One is that leukemia is not a disease of the circulating blood; it is a disease of the leukopoietic system. This is the reason I object very much to gauging treatment entirely on blood studies because you need all the information possible concerning the entire leukopoietic system.

Take for instance the cases of Dr. Portmann. A leukopenic leukemia with a marked hyperplasia of the marrow should be treated as vigorously as if the person has a count of a million white cells. What you are treating is the hyperplasia in the marrow, not the cells that have actually got into the blood stream.

One important point has not been mentioned —about the time to start treatment. I am an internist and not a radiologist, but I think it is a great mistake to treat patients with leukemia by irradiation too early. Many patients can be carried on easily for quite a long time before irradiation is begun.

It makes no difference how high a person's white blood cell count is. The treatment is not curative. You are trying to make the patient have a feeling of well being.

So much in leukemia depends upon the toxemia, of which anemia is probably the best index. A progressive anemia is always an indication for more aggressive treatment. Many hematologists would much rather know what the hemoglobin content is rather than the white blood cell count in treating leukemia.

Determination of the basal metabolic rate has

not helped us much in managing leukemia. A leukemia may be very active without a high metabolic rate.

Dr. Chamberlain has asked how to differentiate acute lymphocytic leukemia and acute leukemia of the myelogenous group. That is a very embarrassing question for a hematologist, but in most cases if one sees the patient from both the blood and clinical standpoint (and it has been my good fortune to see them in both the laboratory and in the clinic), one can usually be fairly sure whether the disease is lymphoid or myeloid in origin. The general pattern of the cells present helps greatly. An immature cell is a lymphoblast, a myeloblast, or a monoblast. What kind of company does that cell keep? One can usually tell by the bone marrow findings and other cells present the origin of the immature cell better than by the characteristics of the individual cell.

Dr. Martin asked about agnogenic myeloid hyperplasia. After all, the marrow is a very hyperactive part of the body. Think of the billions of white blood cells that are formed every day, the great speed with which they are circulating and being destroyed! Agnogenic myeloid hyperplasia is a terminal state in which the normal physiologic control is lost and abnormal cells get into the circulation. This is not leukemia, and there is no reason whatsoever to treat such cases as leukemia.

I wish very much that the word "aleukemia" were dropped entirely from the terminology of hematology. Cases so designated are really examples of leukopenic leukemia. Why call them aleukemia?

A ROENTGEN STUDY OF CHRONIC PULMONARY COCCIDIOIDOMYCOSIS

By LIEUTENANT COLONEL H. W. JAMISON
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ALTHOUGH coccidioidomycosis in its malignant disseminated form was recognized as a clinical entity as early as 1892 by Wernicke and Posadas of Argentina, it is only in the past decade that the far more common benign or "primary" form of disease has been recognized. For many years it had been known that the incidence of erythema nodosum was much higher in the San Joaquin Valley of California than in other parts of the country. When associated with an influenza-like respiratory infection the disease was variously referred to as San Joaquin Valley fever, valley fever, desert fever, or desert rheumatism. All patients were thought to recover. In 1935 Gifford[12] and Dickson[8] were able to demonstrate that *Coccidioides immitis* was the causative organism in this disease. Dickson thereupon suggested that the name "coccidioidomycosis" be employed for both forms of the disease, classifying as primary, the acute initial infection, and progressive or secondary, the classical coccidioidal granuloma.

Up to 1936 the total number of cases of coccidioidomycosis reported in California was only 450 of whom 224 had died. Yet Dickson found by sending a questionnaire to 75 physicians practicing in the San Joaquin Valley that a total of 354 patients with valley fever associated with erythema nodosum had been seen in the previous eighteen months (January, 1936–May, 1937). All but one of these patients had recovered spontaneously. In a similar period (December, 1937–May, 1939) Dr. Charles E. Smith of Stanford, investigating the disease in Kern and Tulare counties, saw 432 cases of acute coccidioidomycosis with erythema nodosum or erythema multiforme. The illness in every case was associated with either a positive sputum culture or a positive coccidioidin skin test. Gifford and her associates found by testing 2,718 school children in Kern County that 55 per cent gave positive coccidioidin skin tests. The percentage rose from 17 per cent for those of less than one year residence in the county to 77 per cent for those having lived in the county ten years or more. In one group of 143 positive reactors only 4 gave a history of erythema nodosum; in another group, only one of 76 positive reactors had had erythema nodosum. Smith calculated on this basis that the 432 cases with erythema nodosum that he had seen must have represented some 8,000–10,000 infections. Thus, a high incidence of coccidioidal infection of the population, particularly of the sublinical type, was demonstrated in this endemic area.

With the advent of war and establishment of Army Air Fields throughout the endemic Southwest, the military implications of coccidioidomycosis were quickly appreciated, and a control program was set up under the Army Air Forces Western Flying Training Command. It was decided to skin test all new personnel arriving at Army Air Fields under this command. Negative reactors were retested six months later. Chest roentgenograms on positive reactors were carefully rechecked for any evidence of the disease. In addition, a syllabus on coccidioidomycosis was prepared and distributed in 1942 to all Army Air Fields in the Western Flying Training Command. All Medical Corps officers of these Fields were alerted to recognize the disease. As a result, several hundred clinical cases were discovered, as well as several thousand subclinical cases having a positive coccidioidin skin test. All clinical cases were hospitalized until evidences of activity had disappeared. All were checked periodically by roentgenograms. In most cases, the

acute febrile illness was self limited and of short duration, but a small percentage of infections persisted for many weeks or months, and a few terminated fatally. Patients whose infections were unusually prolonged or severe were generally transferred to the Santa Ana Army Air Base Regional Hospital for further observation and care. This group forms the basis of the present study.

ETIOLOGY AND EPIDEMIOLOGY

The causative organism was at first thought to be a protozoan. Rixford and Gilchrist, in reporting the first 2 California cases in 1896, so described it. In 1900, however, Ophuls and Moffitt were able to demonstrate its fungus nature. The name, *Coccidioides immitis*, suggested in 1896 by Dr. Charles Wardell Stiles then of the Bureau of Animal Industry, was retained nevertheless.

In its parasitic stage, as seen in tissue sections, the organism is a spherule 5 to 80 or more microns in diameter with a thick double contoured refractile capsule. It enlarges as it matures, and its granular protoplasm breaks up into a large number of endospores which are released when the spherule bursts. The released endospores then enlarge independently to form mature spherules, thus repeating the cycle.

The vegetative phase appears as a cottony white fungus which grows with great freedom on many media. It reproduces by budding and fragmentation of the mycelia. Although it is readily cultured in the laboratory, little is known of its occurrence in nature. It is generally assumed that the fungus grows in the soil or on vegetation during the rainy season and that during the dry season the chlamydospores break from the fungus and are scattered with the wind. This theory is in accord with the known seasonal incidence of the disease which is lowest during the rainy months of December to May and highest during the dry months of August to October. Those whose work brings them in close contact with the soil are most apt to become infected, such as farmers, fruit and cotton pickers, linemen, well diggers, and others. Davis, Smith and Smith[6] reported a group of seven Stanford students who developed the disease after digging out a rattlesnake in the Panoche Valley. *Coccidioides* was recovered from the soil of the rattlesnake nest. Emmons[10] suggests that small rodents such as pocket mice and kangaroo rats may be an important natural

Fig. 1. Acute pneumonic type of coccidioidomycosis, lower right lung; complete resolution within three weeks. Symptoms: malaise, mild substernal pain, cough. Temperature 99–100° F., six days. Leukocyte count 8,700, with neutrophils 78 per cent, eosinophils 2 per cent. Sedimentation rate 50. Coccidioidin test positive.

reservoir for the disease. In a high percentage of these animals coccidioidal organisms could be isolated from the characteristic nodular lung foci.

All observers are agreed that direct person to person transmission of the disease does not occur. The disease is acquired almost solely by inhalation of air contaminated by chlamydospores. Rarely, direct infection through abrasions of the skin have been reported, but no case of infection via the gastrointestinal tract has been recorded.

The disease is endemic throughout much of the arid Southwest including the great central valley of California (the San Joaquin) especially south of Fresno, the

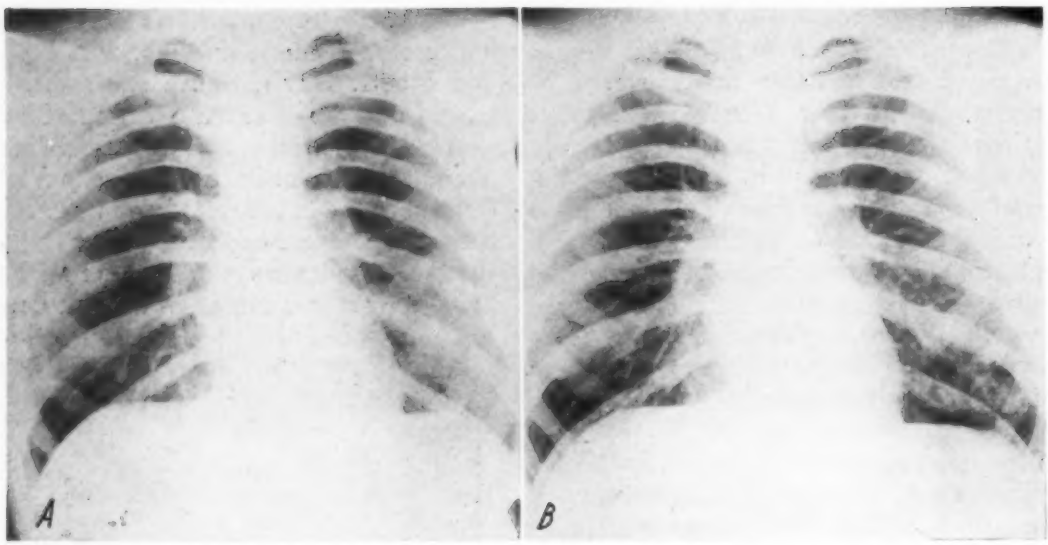


FIG. 2. *A*, coccidioidal pneumonitis, left base. Symptoms: fever, backache, substernal and lower left chest pain, five days, asymptomatic thereafter. Coccidioidin test positive. Complement fixation test positive 1:2. *B*, nodular coccidioidal focus with small central cavity, left base, at site of pneumonitis shown in *A*, twelve days later. Patient asymptomatic. Lesion unchanged over a three and one-fourth month period of observation.

whole of Arizona but especially the regions about Phoenix and Tucson, Southwest Nevada, and parts of New Mexico and Western Texas. Sporadic cases have been reported from the Midwest, Idaho, Utah, the Chaco region of Argentina, Bolivia, Paraquay, Brazil, Northern Mexico, Hawaii and Italy.

ACUTE PRIMARY COCCIDIOIDOMYCOSIS

After a period of ten to fourteen days following inhalation of air contaminated with coccidioidal spores, the patient may, or may not, have clinical symptoms. Most residents of endemic areas never develop symptoms of any kind, the only evidence of the disease being a positive coccidioidin skin test. Others develop an acute febrile illness often misdiagnosed as a severe "cold" or "flu" or "pneumonia." The patient complains of backache, headache or general aching, of marked weakness, loss of appetite and various indefinite gastrointestinal disturbances. Cough begins early and is usually of a dry irritating type, but small amounts of sputum may be raised. A most striking feature, and especially significant in differentiating the disease from the more common respiratory infections, is the occurrence of chest pain in a very high percentage of individuals (87 per cent of one series of 30 acute cases). This varies from a dull constricting substernal type to a very sharp knife-like pain which may suggest coronary occlusion or even fractured ribs. Tenderness to pressure is often encountered over the painful area. The temperature is of a spiking type with afternoon rise, usually to 100° to 102° F. The white count is elevated in most cases averaging 10,000 to 12,000 (6,000–16,000), the neutrophil percentage is mildly increased and eosinophilia of 3 to 15 per cent may be present. Usually after three to ten days the temperature falls to normal, and the patient feels well except for weakness and perhaps residual chest pain. Then, one to two weeks later, painful nodules may develop on the shins and elsewhere characteristic of erythema nodosum. In other cases, macular, papular or vesicular lesions of erythema multiforme may appear. Acute arthritis and conjunctivitis are often associated with these allergic skin manifesta-

tions. The skin lesions are said to occur in 2 to 5 per cent of all cases,[20] but the incidence is evidently much higher in clinically diagnosed cases (19 per cent of 85 cases reported by Goldstein and MacDonald[13]; 17 per cent of our series). Following the acute illness the patient frequently feels weak and easily fatigued for many weeks or months thereafter.

A roentgenogram of the chest taken at the time of hospital admission will show characteristic roentgen findings in at least 4 out of 5 patients. Infiltrations vary in extent from the slightest fuzzy thickening of hilar shadows to extensive consolidations occupying one-third to one-half a lung field. These infiltrations are mostly unilateral, homogeneous, usually hilar or basal in location and show little tendency to lobar distribution. They vary in density from the lightest veil-like haze to consolidations approaching but rarely equalling that of lobar pneumonia. The appearance resembles that of the primary atypical pneumonias, being more uniform, less patchy, more circumscribed than the usual bacterial bronchopneumonias. The hilar type infiltration resolves most rapidly, usually within one to two weeks. The very soft parenchymal infiltrations also resolve rapidly and completely, usually by the second to fourth week, while the denser consolidations generally clear more slowly and give rise to a majority of the persistent infections. Mediastinal or hilar adenopathy occasionally accompanies the more severe of these acute primary infections, but when it does occur, it is usually transitory and mild in degree. Pleural effusion is encountered in approximately one-fifth of all acute primary cases but ordinarily is so small in amount as to scarcely fill the costophrenic angle; it resolves rapidly and completely.

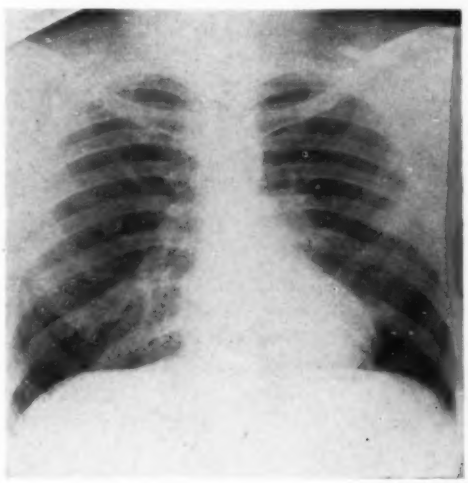


Fig. 3. Nodular coccidioidal focus, left mid-lung, unchanged over eight month period of observation. Sputum originally positive for *Coccidioides immitis*. Coccidioidin test positive. Patient asymptomatic except for occasional sharp left chest pains; leads active, normal life.

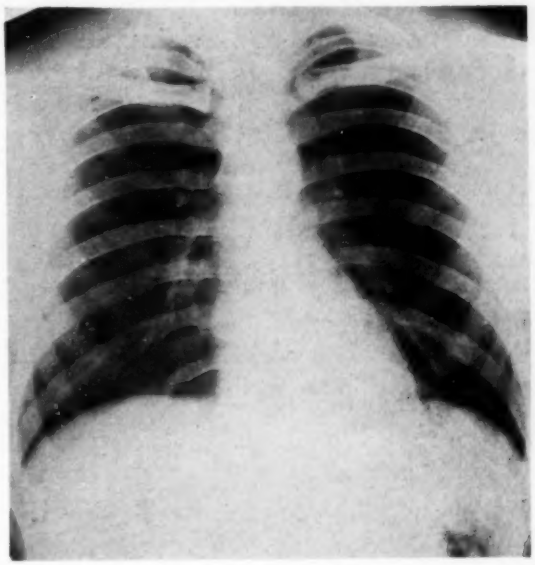


Fig. 4. Nodular coccidioidal focus, right apex, unchanged over nine and one-half month period of observations. Discovered on routine roentgenogram. Coccidioidin test positive. Occasional chest pain, slight cough.

DIAGNOSIS

The diagnosis of coccidioidomycosis depends on (1) a positive coccidioidin skin test plus a diagnostically characteristic roentgenogram and a compatible clinical history, (2) positive serologic tests, or (3) recovery of the fungus from the sputum (or, in disseminated cases, from accessible nodes or abscesses). Kessel[15] and others have shown that the coccidioidin test has a

high degree of specificity and parallels in many respects the tuberculin test in its mode of action. A positive reaction indicates that the patient has had at one time a coccidioidal infection, and does not necessarily imply that a present illness is due to this infection. On the other hand, a negative test excludes the disease in all but terminal cases.

Serologic tests have proved a very valuable aid, both from the standpoint of diagnosis and prognosis. Precipitin and complement fixing antibodies appear in the blood early in the course of the disease. Usually in the early stages precipitins are present in higher dilution but rapidly disappear. The complement fixation titer falls off more gradually. With resolution or focalization of lung infections, complement fixation disappears or is present in low dilution; with dissemination, the titer remains at a constantly high level or increases to the "danger" range of 1:64 to 1:128 or more.

Recovery of the fungus from the sputum is a difficult and tedious process, and in acute primary cases the sputum is often so scanty as to make this procedure impractical. Examination of sputum under a coverslip in the fresh state is very unsatisfactory, since fat droplets and other artefacts may readily simulate the organism. Culture on Sabouraud's medium followed by guinea pig or mouse inoculation is the only reliable method of recovering and identifying the organism.

PERSISTENT COCCIDIOIDAL INFECTIONS

In cases with persistent coccidioidal infections the clinical picture parallels quite closely the findings shown by roentgenogram. Persistent infections may thus conveniently be classified and discussed according to predominant roentgen manifestations, as follows:

1. Nodular parenchymal foci.
2. Cyst-like cavities.
3. Persistent pneumonitis.
4. Mediastinal and hilar adenopathy.
5. Pleural effusion.
6. Miliary lung involvement, metastatic

Fig. 5. *A*, coccidioidal pneumonitis, right mid-lung. Infiltration had largely but not completely cleared on roentgenograms taken two weeks later. No further roentgenograms were taken until ten months later. *B*, coccidioidal cavity, right mid-lung, at site of pneumonitis shown in *A*, twelve and one-half months later. *Coccidioides immitis* recovered from the sputum. Coccidioidin test positive.

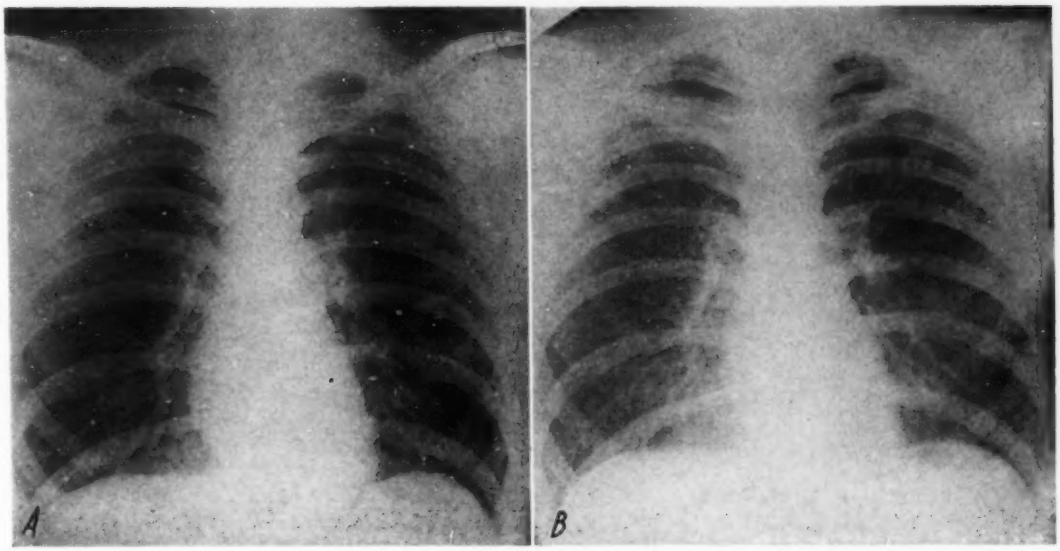


Fig. 6. *A*, coccidioidal cavity, right subapex, discovered on routine roentgen examination. Patient asymptomatic. Coccidioidin test positive. *B*, coccidioidal cavity shown in *A* beginning to disappear eight months later.

bone foci and other evidences of dissemination.

Of 96 cases of persistent infection followed at the Santa Ana Army Air Base Regional Hospital for periods of from two to twenty-one months, 23 cases were of the nodular type, 35 were cyst-like cavities, 21 were persistent pneumonites, mediastinal adenopathy was predominant in 2 cases, pleural effusion was outstanding in 3, and the remaining 12 cases were disseminated. Only those patients whose roentgenograms showed evidence of infection beyond a two month period, constituting some 10 to 15 per cent of clinical cases, are included in this group of persistent infections.

NODULAR PARENCHYMAL FOCI

The nodular parenchymal foci were discovered, in a majority of cases, on routine roentgenograms. Fifteen of the 23 cases of this type were so discovered. Of the 15 cases, 3 were found on questioning to have had occasional chest pains, 4 had felt weak and easily fatigued, and the others had been symptom free. Eight gave a history of an acute febrile illness two to ten months previously. Three additional cases were discovered by chest roentgenograms taken because of patient's complaint of chest pain in 2 instances and abnormal fatigability in the other. The coccidioidin skin test was positive in all these cases, the temperature was normal in all, and sedimentation rate was mildly elevated in only 3 cases. Complement fixing antibodies were present in low dilution in 2 of 6 cases in which it was tested for.

Only 4 patients were followed directly through from a preliminary stage of pneumonitis to nodule formation. In all 4 cases the initial acute illness was of relatively short duration and comparatively mild symptomatically. Temperatures varied from 99° to 101° F. and lasted three to seven days. Infiltrations, which at first were more or less diffuse, tended to round out with decrease in size leaving solitary well circumscribed nodules at the sites of the previous zones of pneumonitis. The elapsed time from the initial pneumonitis to nodule formation varied from ten days to three months, averaging five to six weeks.

The nodules in all but one instance were

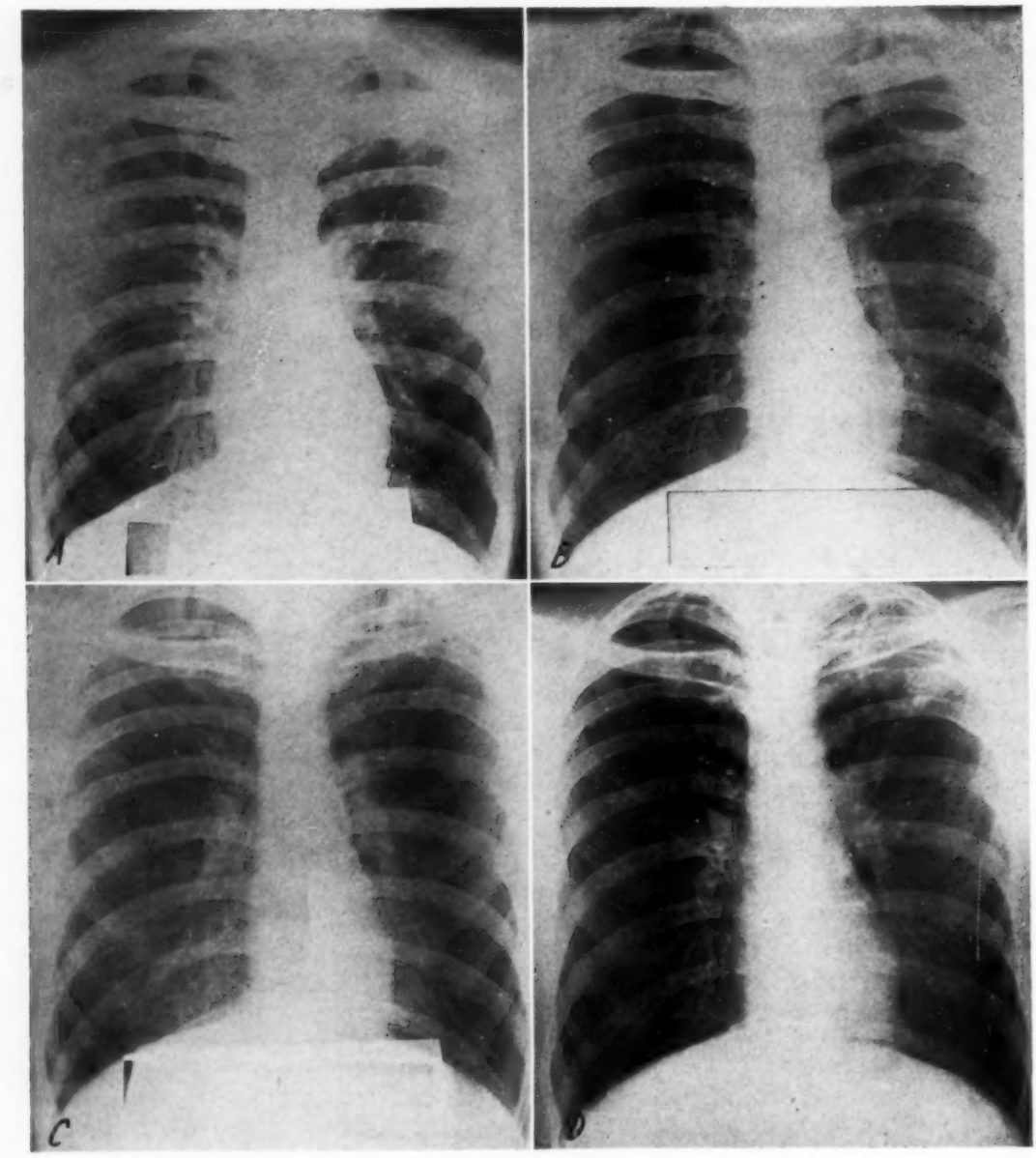


FIG. 7. *A*, small coccidioidal focus, left apex, discovered on routine roentgenogram. Patient practically asymptomatic, slight cough. Normal temperature. Coccidioidin test positive. Complement fixation test positive 1:4. Sedimentation rate elevated five months, normal thereafter. *B*, coccidioidal cavity, left apex, four and three-fourths months after *A*. *Coccidioides immitis* recovered from sputum. Patient remained essentially symptom free, raised small amounts of purulent sputum. Temperature normal. Leukocyte count 5,000 to 11,700, eosinophils 11 to 14 per cent. *C*, coccidioidal cavity shown in *B* much smaller three months later. *D*, re-enlargement of coccidioidal cavity two months after *C*. *E*, coccidioidal cavity shown in *D* had disappeared after three weeks.

single. They were located in the apical or subapical regions in 2, the mid-lung in 12, the lower lung in 7, and were multiple and generalized in one. They averaged 2.0 cm. in diameter, varying from 0.8 to 4.2 cm. They were strikingly similar in appearance to solitary neoplastic metastases, or uncalcified primary tuberculous foci. In the 1 case in which multiple nodular foci were present the resemblance to extensive metastatic malignancy was pronounced. In this instance, however, each of the nodular lesions was preceded by a zone of pneumonitis, and some of the nodules later developed central cavitation.

The period of time that the nodules were under observation was insufficient to give a clue as to their ultimate fate. Over an average observation period of six and one-half months (one to nineteen months) only a single one of these foci had disappeared, four had decreased an average of 3 mm. in diameter and the remaining seventeen had changed not at all. From other studies, however, it is evident that some, at least, go on to eventual calcification. *Coccidioides immitis* has been recovered from calcified pulmonary nodules at autopsy (Cox and Smith[4]). Aronson and his coworkers[1] found a high incidence of calcified nodules in Indian children living near Phoenix, Arizona, who failed to react to tuberculin but did react to coccidioidin. Failure to react to tuberculin in those showing calcified nodules could not be attributed to anergy since in 56 of 62 such persons the tuberculin test became positive one year after the intracutaneous injection of B.C.G. vaccine. The inference was strong that these calcified nodules were coccidioidal in origin.

COCCIDIOIDAL CAVITIES

Coccidioidal cavities, like the nodular foci described, are frequently discovered on routine chest roentgenograms without prior clinical evidence of disease. Thirteen of 35 cases were so discovered. Five of the 13 were found on questioning to have had occasional chest pains or had felt weak and under par. Six additional patients were discovered to have cavities by roentgenograms taken because of symptoms of chest pain in 3, hemoptysis in 2, and weakness and fatigability in one. In 11 cases, cavity formation was seen to follow directly on a preceding stage of pneumonitis. In 5 additional cases, cavities were observed to develop by central excavation of preexisting nodular foci.

The acute illness preceding cavity formation was generally more prolonged and

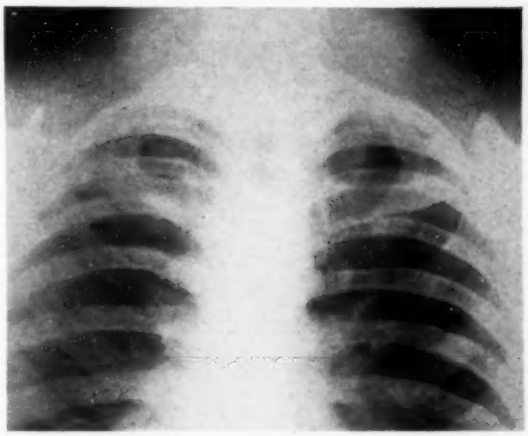
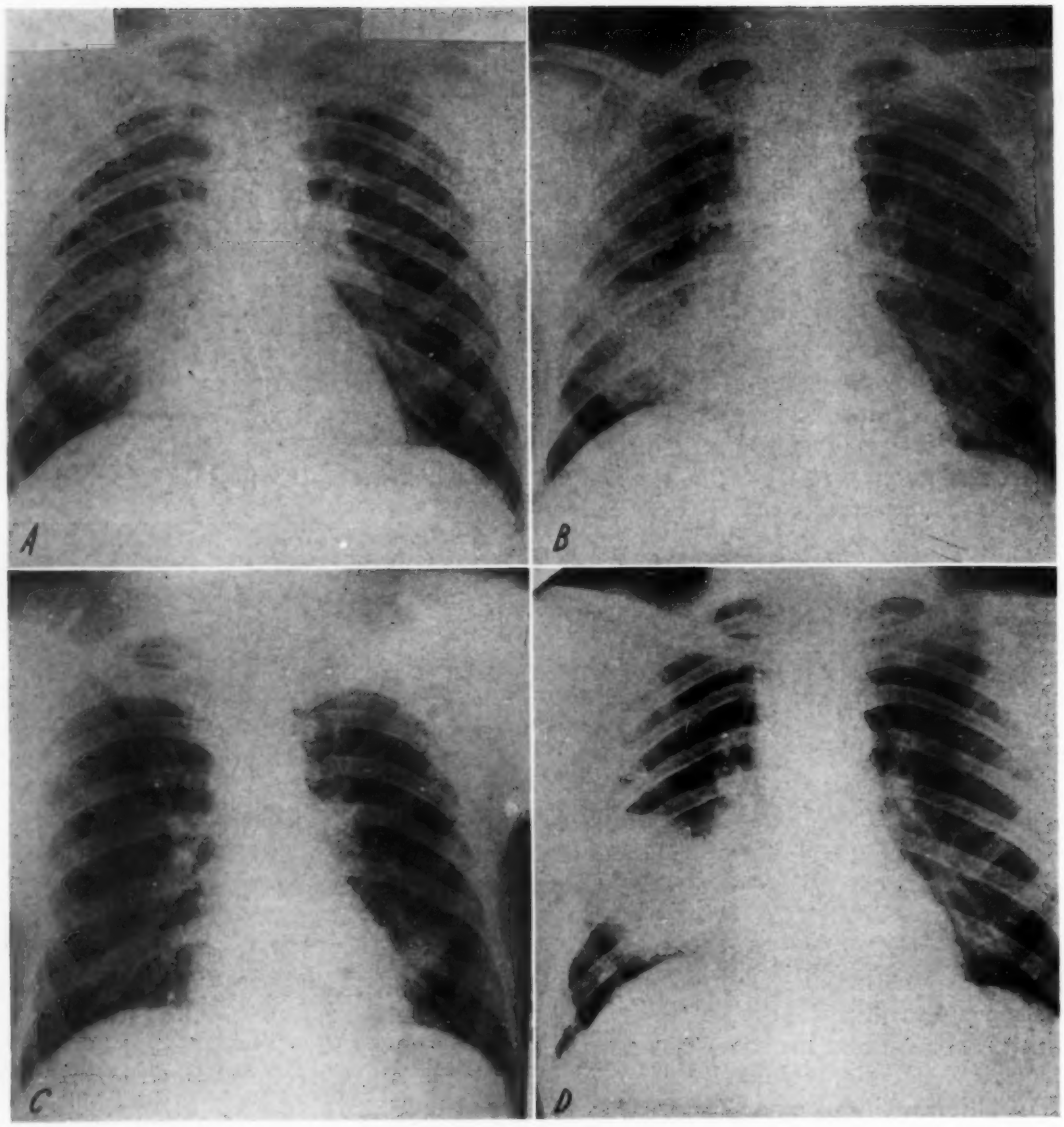


Fig. 8. Persistent coccidioidal pneumonitis, left apex. Lesion discovered on routine roentgenogram. Patient asymptomatic. Temperature normal. Acute febrile illness with erythema nodosum, four months previously. Coccidioidin test strongly positive. Tuberculin test negative. Sedimentation rate 10–20. Lesion unchanged over eight and one-half months of observation.

severe than in cases later developing nodules. Temperatures varied from 100° to 103° F. and averaged nine days in duration. The acute symptoms of severe malaise, cough, chest pain, general aching, and so forth, were generally present over a two to four week period, subsiding thereafter, usually coincident with the appearance of cavities as shown by the roentgenogram. That such cavities then represent latent focalized infections is shown by the fact that, in the great majority of cases, temperature, white blood cell count and sedimentation rate fall to normal limits, and antibodies disappear from the blood or remain in low dilution soon after the cavity



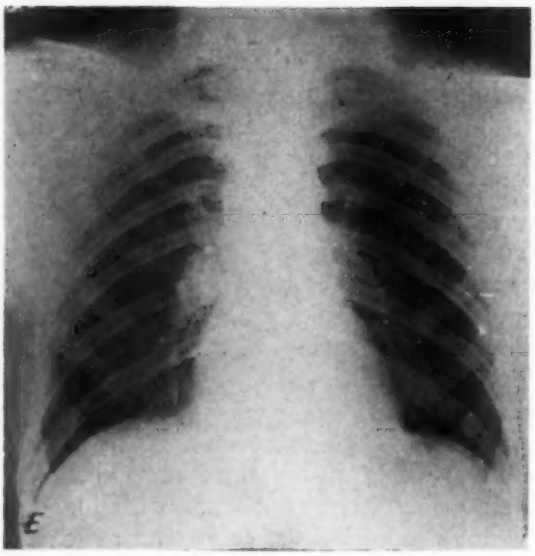


FIG. 9. *A*, coccidioidal pneumonitis with mediastinal adenopathy. Patient severely ill with general aching, sharp chest pain, skin lesions (erythema multiforme?). Temperature 103–105° F. for one month, then 99–101° F. for another month. Leukocyte count 23,350, with neutrophils 42 per cent, eosinophils 22 per cent. Complement fixation positive 1:32. Sedimentation rate 51. *Coccidioides immitis* recovered from sputum.

B, infiltration and mediastinal adenopathy shown in *A* have markedly increased after two months. Temperature 100° F. Leukocyte count 13,000, eosinophils 5 per cent. Biopsy of subcutaneous nodules of shoulders and forearms which appeared after one month showed granulomatous structure with giant cells and eosinophils compatible with coccidioidomycosis. These lesions later gradually disappeared.

C, infiltration shown in *B* has markedly regressed after two months.

D, re-consolidation of the right middle lobe, four months after *C*, nine months from onset of coccidioidomycosis. Patient returned from leave with headache, chest pain, cough, temperature 100–103° F.

E, infiltration shown in *D* has cleared after one and one half months. Adenopathy has largely disappeared. Complete recovery.

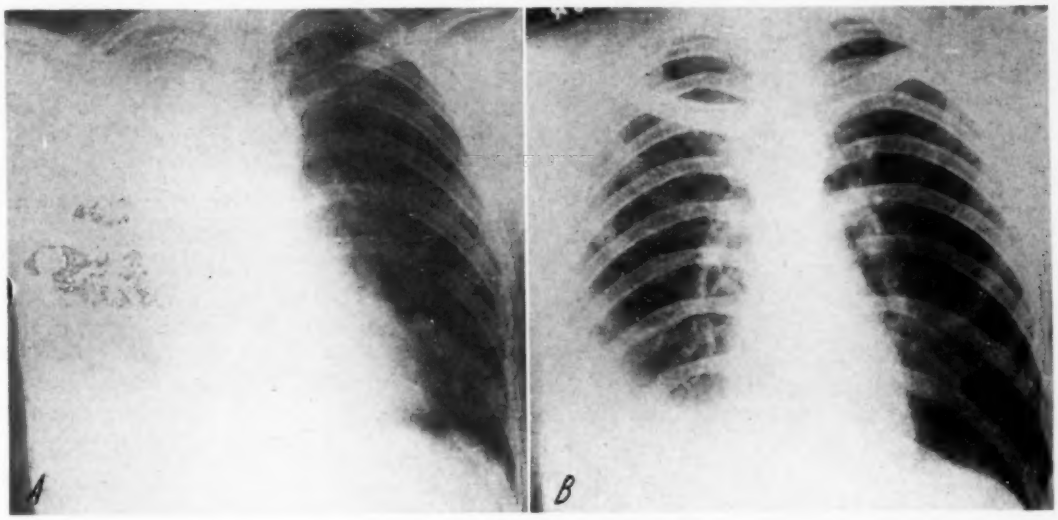


FIG. 10. *A*, massive coccidioidal pleural effusion. Coccidioidin and complement fixation tests positive. Right chest pain. *B*, effusion shown in *A* has decreased after four months. No parenchymal infiltration demonstrated at any time.

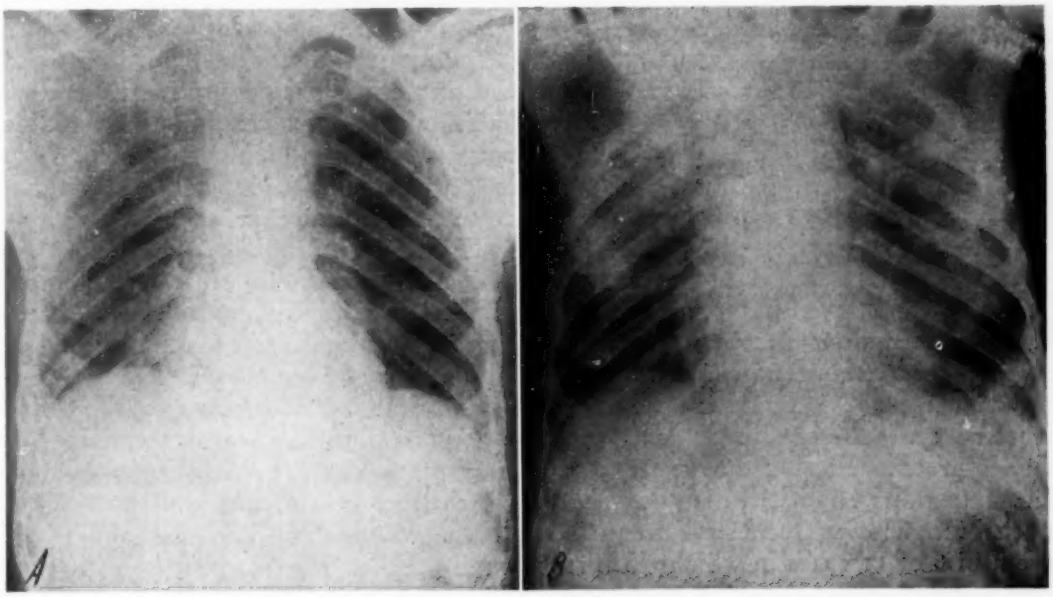


FIG. 11. *A*, small amount of coccidioidal pneumonitis at left costophrenic angle and right mediobasal region with mediastinal adenopathy. Negro admitted with complaints of feverishness, fatigue, malaise, tender "lumps" 3–5 cm. in diameter on lower chest, sternum, abdomen and extremities. Temperature 102–103° F. Complement fixation titer as high as 1:128; sedimentation rate as high as 98. *Coccidioides immitis* recovered from subcutaneous nodules by culture and guinea pig inoculation. *B*, extensive partly confluent miliary infiltrations with mediastinal adenopathy, two months after condition shown in *A*. Many punched out foci of bone destruction in ribs, scapula and humerus. Course steadily retrogressive with great weakness, severe weight loss, occasional headaches, and anorexia to time of death three months from onset.

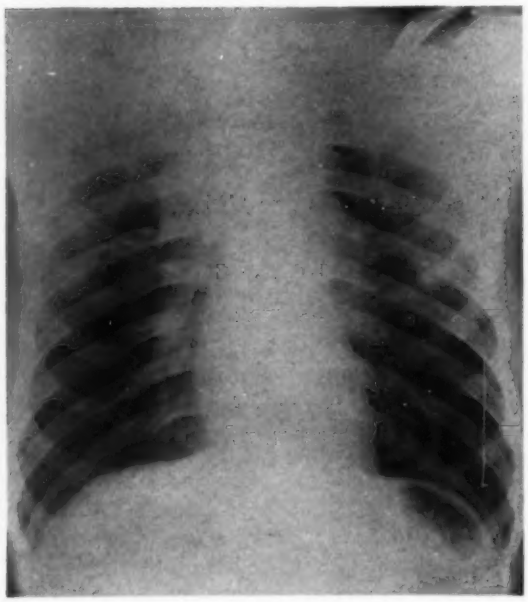


Fig. 12. Massive mediastinal coccidioidal adenopathy. Negro admitted with fever, headache, general malaise, anorexia, followed by persistent cough, marked weakness and wasting, dull pain in mid-chest, and cervical adenopathy. *Coccidioides* recovered from cervical nodes. Died in coma seven months from onset. Temperature 101–103° F., leukocyte count 13,000–17,000 with neutrophils 68 per cent; erythrocyte count 3.6 million, hemoglobin 83 per cent. At autopsy necrotic mediastinal nodes found to have eroded into esophagus. Also involvement of meninges, kidneys and heart.

appears. Moreover, clinical signs of activity are usually absent even in presence of considerable fluctuations in cavity size and wall thickness. About half the patients, however, complain of persistent weakness or intermittent chest pain so long as a cavity is present. Four of our patients developed hemoptysis with their cavities, and the fungus was recovered from the sputum in 6 of 11 cases in which this procedure was attempted.

Infiltrations preceding cavitation were homogeneous zones of consolidation 2 to 10 cm. in diameter which tended to round out with decrease in size prior to excavation. The average elapsed time from the appearance of infiltration to development of cavity was three and one-half weeks (ten days to eight weeks). Mediastinal adenopathy accompanied 4 of the 11 precavity infiltrations but, in each case, disappeared as the cavities developed.

Cavities were single in every case, located in the upper lung field in 11, the mid-lung in 15, and the lower lung field in 9 cases. Most cavities were of a very thin-walled type without surrounding infiltration, presenting a characteristic ring-like or cystic appearance. Cavities which developed through central excavation of nodular foci were usually smaller in size and thicker walled having a doughnut-like appearance. These cavities required an average of three months to develop (one to six months).

All cavities were remarkably indolent, slow in evolution, and benign in character. But minor fluctuations in size and wall thickness were recorded in practically all cases. In 8, the fluctuations were of such degree and occurred so rapidly as to strongly suggest ballooning due to air trapping. The cavities were followed roentgenographically for periods of from one to eighteen months, averaging seven and one-half months for the group. During this time only 10 cavities had disappeared, 6 had ended as small nodules and the remaining 19 were essentially unchanged.

The manner in which cavities disappeared was of some interest. Often one side of the wall would appear to melt away leaving a crescentic residuum which then gradually resolved. Some of the larger thinner walled cavities appeared to collapse rapidly over a period of several days either to reappear just as suddenly or to disappear permanently. Less commonly, the cavity gradually diminished in size ending as a small nodule. The 19 cavities still present after an average follow-up period of seven and one-half months were actually slightly greater in average diameter (though thinner walled) than at the time of initial examination. They varied in size from 1 to 8 cm. in diameter, and averaged 2.2 cm. at the onset, while at the time of final observation, the average diameter was 2.6 cm.

Most coccidioidal cavities are so charac-

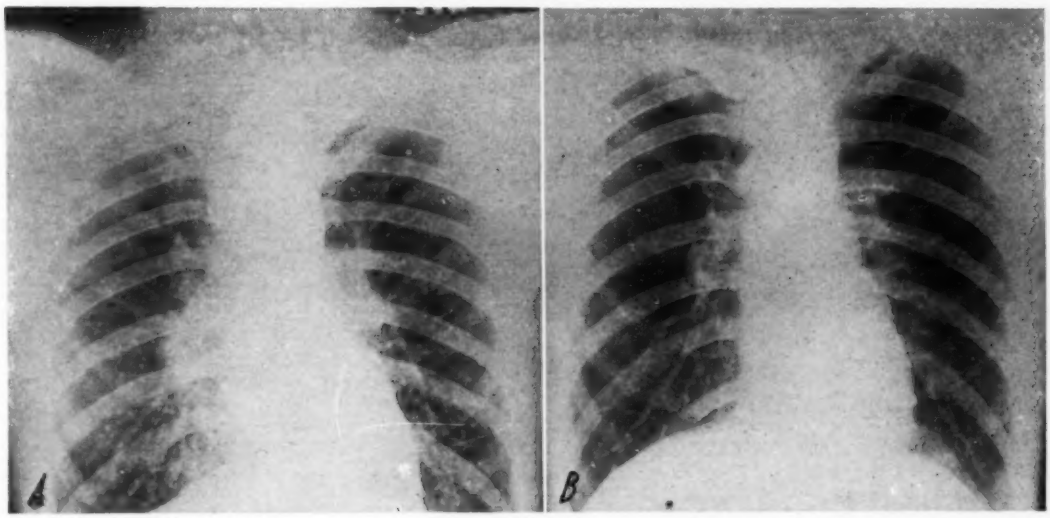


Fig. 13. *A*, mediastinal adenopathy with slight hilar infiltration. White patient admitted with malaise, headache and vomiting. Temperature 100° F. Leukocyte count 9,850, with neutrophils 65 per cent, eosinophils 10 per cent. Sedimentation rate 18–57. Coccidioidin test positive. Increasing headache followed by disorientation and mental confusion. *B*, mediastinal adenopathy and hilar infiltration shown in *A* have disappeared after two and three-fourths months. Patient died of meningitis one week later, three months from date of admission. Mediastinal nodes completely caseous but only slightly enlarged.

teristic in roentgen appearance that they are seldom confused with other conditions when occurring in endemic areas. They have been misdiagnosed as congenital cysts, and in 1 case a lobectomy was performed under this impression. Sante and Hufford[19] have recently described annular lung shadows appearing in pyogenic blood infections which appear remarkably like those of coccidioidomycosis. Three of our 35 coccidioidal cavities contained fluid at intervals, and when fluid containing, were surrounded by infiltration. The appearance at these times resembled that of lung abscesses. Five other cavities which did not contain fluid but were surrounded by infiltration at various times could readily have been mistaken for ulcerative tuberculosis, especially when occurring in the upper lung fields.

PERSISTENT COCCIDIOIDAL PNEUMONITIS

A number of acute primary infiltrations failed either to resolve completely or to focalize as nodular or cystic lesions during the two to six week period usually required for resolution or stabilization. These patients, as a group, were clinically severely ill with marked prostration, malaise, general aching, usually sharp chest pain, and occasionally blood streaked sputum. Temperatures frequently reached levels of 103° to 104° F. during the first several days and persisted thereafter at lower levels for weeks or months (six days to three months: average twenty-nine days). Sedimentation rates were elevated to levels of fifteen to fifty for one to eight months (four and one-half month average). Complement fixing antibodies were present in dilutions of 1:4 to 1:32 initially, falling off after two to six months, and disappearing in all but the most severe infections after six months.

The initial infiltration was often extensive. In 7 of 21 cases consolidations occupied one-third to one-half the lung field, half were moderate in extent (4 to 8 cm. in diameter), while in 5 of the group, infiltrations were small in amount and limited to the hilar regions.

As might be expected, the more extensive, denser infiltrations were slowest to resolve, requiring six to twenty-one months

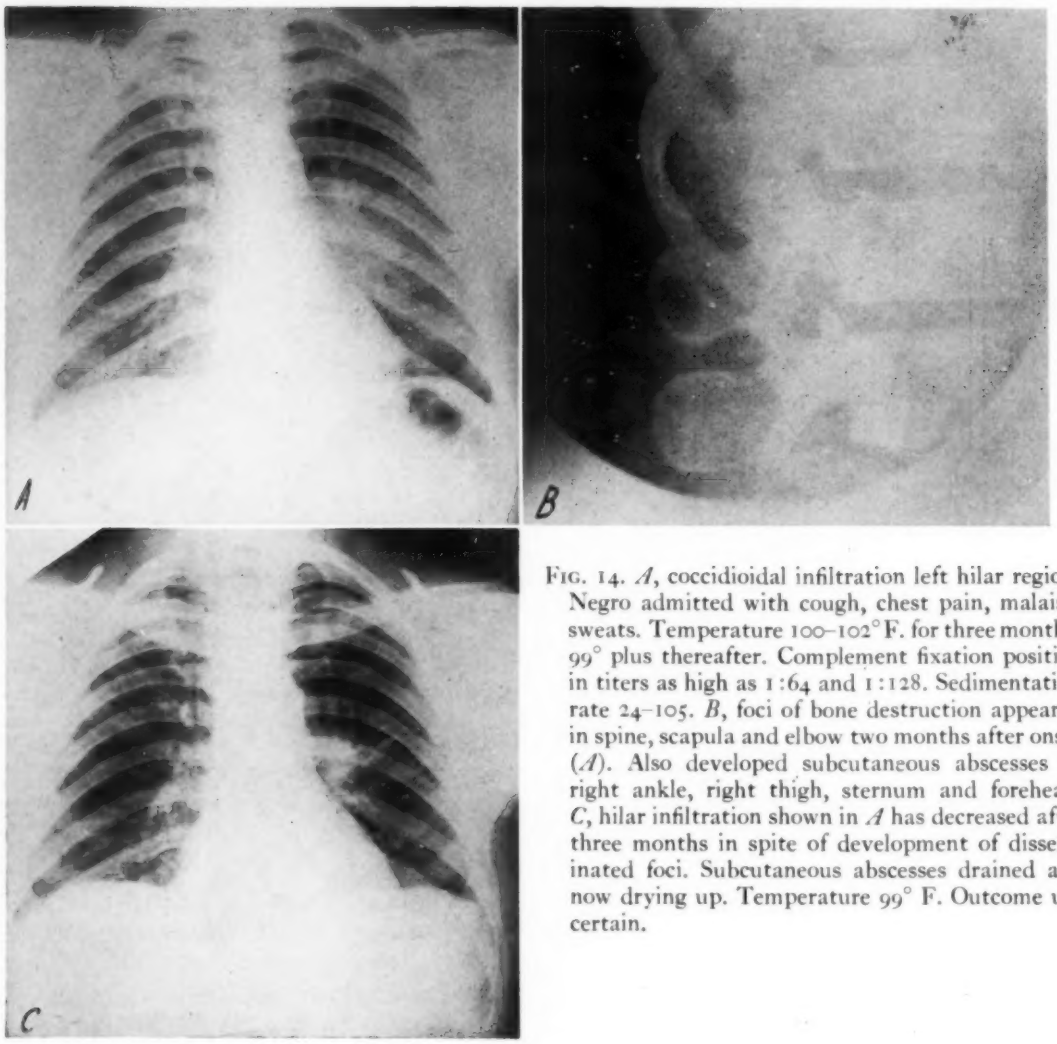


Fig. 14. *A*, coccidioidal infiltration left hilar region. Negro admitted with cough, chest pain, malaise, sweats. Temperature 100–102° F. for three months, 99° plus thereafter. Complement fixation positive in titers as high as 1:64 and 1:128. Sedimentation rate 24–105. *B*, foci of bone destruction appeared in spine, scapula and elbow two months after onset (*A*). Also developed subcutaneous abscesses at right ankle, right thigh, sternum and forehead. *C*, hilar infiltration shown in *A* has decreased after three months in spite of development of disseminated foci. Subcutaneous abscesses drained and now drying up. Temperature 99° F. Outcome uncertain.

to clear, while the smaller hilar infiltrations disappeared after an average interval of three and one-half months. In most cases, resolution was a very gradual but continuous process. Four of the group, however, showed exacerbations and remissions over periods of from four to ten months. In spite of the slow resolution, only 1 of the entire group of 21 showed evidence of fibrosis; the other infiltrations preserved to the very end a soft homogeneous or patchy appearance. Mediastinal and hilar adenopathy accompanied 6 of the 21 persistent infections of this group. In these cases it was of pronounced degree and exceedingly persistent (two to twenty-one months: average eight months), often outlasting the parenchymal infiltration.

MEDIASTINAL ADENOPATHY

In 2 cases, marked mediastinal adenopathy was the only roentgen evidence of disease. Both might readily have been misdiagnosed as Hodgkin's disease from the roentgenograms alone. The clinical illness was moderately severe. Complement fixation was present in titer of 1:16 to 1:32, and the sedimentation rates were at levels of thirty to fifty-four so long as adenopathy persisted, which was two and one-half months in 1 case and three months in the other.

PLEURAL EFFUSION

Pleural effusion was the outstanding characteristic of 3 cases. One of these patients, although developing fluid sufficient to produce complete opacity of one side of the thorax, never at any time showed evidence of parenchymal infiltration. A second developed moderate fluid after an initial transitory basal infiltration. Fluid persisted with fluctuations over a fourteen month period, during which time the temperature was elevated to 99° to 100° F. about one-third of the time and the titer of complement fixation rose as high as 1:128 in the range presenting danger of dissemination. The third patient developed slight pleural fluid in association with a coccidioidal cavity. The cavity disappeared after four months, but fluid persisted and increased, lasting a total of thirteen months. The sedimentation rate was elevated the entire time and was as high as thirty-four after eleven months.

FATAL DISSEMINATED COCCIDIOIDOMYCOSIS

Cases destined to develop fatal dissemination cannot be distinguished at the onset from the usual acute pneumonic cases which subside in two or six weeks leaving no sequelae. Indications of impending dissemination are noted when the temperature fails to subside, the complement fixation titer, instead of decreasing rises to the dangerous heights of 1:64 to 1:128 and the sedimentation rate remains elevated at ranges of from fifty to one hundred. Usually within a few days or weeks of the onset of the acute illness, evidences of disseminated foci become manifest. Subcutaneous fluctuant areas 1 to 4 cm. in diameter may even be found at the time of initial hospital admission, and occasionally the presenting symptoms will be those of meningitis.

After the initial dissemination the course is usually that of progressive quiet cachexia to death some two to nine months later. The patient complains primarily of extreme weakness and fatigue and chest pain which is apt to be dull and central in type but may be sharp and pleuritic. Cough is persistent and especially troublesome at night. Subcutaneous abscesses frequently break down discharging purulent exudate from which coccidioidal organisms are easily recovered. Wasting is severe. The temperature remains elevated during the entire course of the disease, usually ranging from 101° to 103° F., but occasionally reaching levels of 104° to 105° F. White blood counts have varied from 7,500 to 27,200, averaging about 13,000, with neutrophils mildly increased and eosinophils ranging from 1 to 12 per cent. A secondary anemia of varying degree has been present in all cases averaging: hemoglobin 81 per cent, red blood cell count 3.8 million.

The roentgen picture in fatally disseminating coccidioidomycosis is dominated by mediastinal and hilar adenopathy. Parenchymal infiltrations, exclusive of the terminal miliary phase, were small in amount and limited to the hilar regions in 7 of our 9 fatal cases. In 4 of the 9, infiltration actually decreased during the later stages of the disease, and adenopathy decreased in 3 cases. Five of the group developed miliary seeding throughout the lungs during the final three to six weeks of their illness. This miliary infiltration developed, as a rule, much more rapidly, and less uniformly, than in tuberculosis and often became massively confluent. Individual miliary nodules tended to be less sharply circumscribed, more fuzzy in appearance than comparable foci of tuberculosis. Small punched out areas of bone destruction in the ribs, scapulae or clavicles could usually be found within a week or two of the appearance of the miliary lung involvement. The bone foci were similar in appearance to metastatic carcinoma.

The disease was found to be remarkably widespread at autopsy, involving practically every organ of the body. Tracheobronchial lymph nodes were invariably caseous and often showed liquefaction necrosis; mesenteric and cervical nodes were frequently caseous; the lungs were involved in all cases, 5 with miliary seeding,

but in 4 only small local foci could be found; foci of bone destruction were encountered in 7 of 9 patients. The incidence of involvement of other organs in the 9 fatal cases was as follows: spleen, 4; kidneys, 4; meninges, 4; liver, 3; heart, 3; adrenals, 1; pancreas, 1. The histopathologic appearance of individual miliary nodules was similar to that of pulmonary tuberculosis, being composed primarily of epithelioid and giant cells, but there were more polymorphonuclear and eosinophilic cells and more tendency to caseous necrosis than in tuberculosis, and many of the giant cells contained coccidioidal spherules.

DISSEMINATED NON-FATAL CASES

Three of our patients developed extrapulmonary dissemination which they were able to focalize successfully. Certain important differences were noted in these patients and those terminating fatally. In the first place, the clinical signs of activity, while often initially severe, soon diminished or even disappeared; temperature, sedimentation rate and complement fixation titer fell after a few days or weeks. Only 1 of the 3 had visible mediastinal or hilar adenopathy. Finally, the interval from original illness to first appearance of disseminated foci was considerably longer than in the fatal cases, averaging three months, whereas 7 of 9 fatal disseminated cases developed extrathoracic foci (subcutaneous abscesses, bone destruction, meningitis) within the first month of their illness, 4 within the first week.

FACTORS INFLUENCING DISSEMINATION

Individual and racial immunity are unquestionably the most important factors which determine whether or not a coccidioidal infection will disseminate. Smith[22] states that the incidence of disseminated infection is four to seven times higher in males than in females. More important, the dark skinned races such as Negroes, Mexicans, and Filipinos show a much greater tendency to dissemination than do whites. On the basis of Army statistics, not yet authorized for release, Colonel R. V. Lee[16] has shown that fatally disseminating coccidioidomycosis is about one hundred times as likely to occur in a Negro as in a white person. Seven of our 9 fatal cases were in Negroes, only 2 in white persons. Thus the commonly accepted figure of 1 dissemination in 500 coccidioidal infections has no meaning unless related to specific racial groups. The incidence in dark skinned races is much higher.

Little is known as to the mechanism of immunity to coccidioidomycosis in humans. Emmons[10] found a high incidence of circumscribed coccidioidal nodules in pocket mice and kangaroo rats but rarely endosporulating organisms. He demonstrated that suppression of maturation and endosporulation was due to host influence as shown by the fact that when strains of *Coccidioides immitis* from these animals were inoculated into more susceptible animals, endospores were invariably produced in the resulting lesions. Whether similar suppression of endosporulation occurs in resistant humans has not been demonstrated.

Smith[22] has commented on the fact that dissemination, when it occurs in white persons, is more apt to be meningeal in type, whereas Negroes show a higher incidence of multiple subcutaneous abscesses. This observation is borne out in our group of fatal cases. Both deaths in white persons were due to meningitis, while subcutaneous abscesses were found in over half of the Negroes who died.

Roentgenographically, the one invariable finding in our disseminated cases of coccidioidomycosis was the presence of enlarged mediastinal nodes at least sometime during the course of the disease. At autopsy, the tracheobronchial lymph nodes were invariably caseous and often extensively necrotic and liquefied. Thus it would appear that the blood stream infection of disseminated coccidioidomycosis arises, at least in most cases, from caseous tracheobronchial nodes.

It would also seem that dissemination,

when it occurs early, as it does in most cases, is of more ominous significance than dissemination which occurs several weeks or months after the original acute infection. Carter[2] has commented on the relatively benign character of isolated foci which are started by minor injuries such as a bumped finger in apparently healthy individuals.

TREATMENT OF COCCIDIOIDOMYCOSIS

The treatment of coccidioidomycosis should correspond to the type and severity of infection. The acute benign form of the disease, constituting the great majority of cases, requires no other care than symptomatic treatment and bed rest until the lungs clear and sedimentation rate returns to normal. Patients with nodular foci should be allowed to carry on a normal active life. Patients with coccidioidal cavities require closer supervision and restriction of activities, but it is questionable whether prolonged hospitalization to time of cavity closure is necessary or advisable. Collapse therapy seems hardly justified in any of these cases with the exception of those patients with repeated and extensive hemoptysis. Patients who have persistent pneumonitis should be hospitalized until all clinical signs of activity (elevated temperature, sedimentation rate, complement fixation) have disappeared and mediastinal adenopathy, at least, has vanished completely. No form of treatment seems to materially affect the course of the disseminated cases. Bed rest, high vitamin and high caloric diet are certainly indicated, but all drugs so far employed have proved of no avail. Some claims have been made for vaccine therapy, but results have not been such as to inspire confidence to date.

SUMMARY

1. The history of coccidioidomycosis is briefly discussed, especially in regard to developments during the past decade. The epidemiology and pathogenesis of the disease are also briefly described.

2. The clinical features of the disease are discussed primarily from the standpoint of differentiating and specific characteristics which distinguish the disease from other acute and chronic pulmonary infections. The coccidioidin skin test is shown to have a high degree of specificity and parallels the tuberculin test in its mode of action. Precipitin and complement fixation tests have proved valuable, not only from the standpoint of diagnosis but also as regards prognosis.

3. Ninety-six coccidioidal pulmonary infections which persisted for months or years following the acute initial phase of the disease are discussed according to predominant roentgen manifestation, as follows:

(1) Nodular parenchymal foci.
(2) Cyst-like cavities.
(3) Persistent pneumonitis.
(4) Mediastinal and hilar adenopathy.
(5) Pleural effusion.
(6) Miliary lung involvement, metastatic bone foci and other evidences of dissemination.

4. The roentgen findings are correlated with associated clinical history. Twenty-three nodular and thirty-five cystic foci were shown to be extremely indolent, benign in character and slow in evolution. Twenty-one patients with persistent pneumonitis required prolonged hospitalization over many months. Mediastinal adenopathy was the predominant roentgen characteristic of nine fatally disseminated cases until the terminal stage of miliary spread.

5. Factors which influence dissemination are discussed with emphasis on the racial factor. (Negroes are about one hundred times as likely to develop fatal disseminated coccidioidomycosis as white persons.) White persons are more apt to develop a meningeal type of coccidioidal dissemination, while Negroes show a higher incidence of subcutaneous abscesses. Dissemination, when it occurs late, appears to be of less ominous prognostic significance than when occurring within the first few days or weeks of the initial acute illness.

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THE MYELOGRAPHIC DIAGNOSIS OF EXTRA-MEDULLARY CERVICAL SPINAL CORD TUMORS*

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INTRODUCTION

THE usual roentgenologic approach to the diagnosis of tumors within the cervical spinal canal is a search for pressure effects on the vertebrae. The presence of an expanding lesion within the cervical spinal canal may be suggested by widening of the interpedicular spaces, destruction or rarefaction of the laminae and pedicles and changes in the interveterbral foramina, but these are usually late manifestations. Until quite recently myelography of the cervical spinal canal was considered a rather difficult, not to say hazardous procedure. The chief objections to the procedure were the possible entrance of lipiodol into the cranial cavity and the physical difficulties incident to roentgenoscoping and maintaining a patient in the inverted position. Pantopaque myelography[3] makes it possible to explore further the cervical canal roentgenologically with an innocuous, slowly absorbable contrast medium, so that the diagnosis of intraspinal tumor masses in the cervical canal may be made before visible changes occur in the vertebrae. This communication reports the myelographic findings in 5 patients with extramedullary tumors of the cervical spinal cord or nerve roots in whom the direct roentgenograms were normal.

TECHNIQUE

Myelography of the cervical spine may be performed with a minimum of discomfort to the patient. A stock model motor-driven tilt table which may be tilted 10 degrees head downward and which is equipped for roentgenoscopy and spot film roentgenography is necessary. We believe it essential to obtain spot roentgenograms under roentgenoscopic control as quickly as possible. The observer must always keep in mind the increased hazards to himself incident to prolonged roentgenoscopy and spot film roentgenography, and avail himself of all possible safeguards.

We have found 3 cubic centimeters of pantopaque injected into the lumbar subarachnoid space adequate. Others use 6 cc. and prefer to aspirate it after examination.[5] The oil column must be maintained in as homogeneous a mass as possible The patient, placed in the prone position with his face turned to one side, is first tilted so that the oil gathers in the lumbar sac. Then he is gradually inverted so that he is head downwards 10 degrees from the horizontal and the passage of pantopaque is watched roentgenoscopically. When this position is reached the oil column usually halts at the level of the first lumbar vertebra. The column may be advanced an additional 3 or 4 cm. by requesting the patient to strain.[1] When the pantopaque has reached the highest level it can with the patient still in this position, he is requested to assume gradually the knee-chest position, and the passage of the oil through the thoracic canal is watched. Streaking and globulation of the column can be kept to a minimum if the hips are gently elevated and the shoulders kept in contact with the table top so that the flow of oil through the thoracic canal is slow. Even though all precautions are observed it is not unusual for the column to break into large streaks and globules, and this should not be confused with organic disease. When the pantopaque reaches the upper thoracic region the patient is returned to the prone position and the table is tilted slightly caudad towards the horizontal. The oil is then permitted to collect

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in the lower cervical canal. As this region is entered the column first assumes a "U" configuration and then divides into two lateral ribbons of greater density between which the remainder of the oil collects. The "U" configuration is transitory and is not to be confused with intrinsic disease at the level of the sixth or seventh cervical vertebra.[2] If the axillary pouches are poorly outlined, they can be filled to better advantage by turning the patient's neck slightly into the oblique position. Occasionally the axillary sleeves fill poorly in normal spines, particularly when the flow of pantopaque through the cervical canal is rapid. Filling defects are considered of diagnostic importance only when confined to one region and when the other pouches are well visualized. The defect must be constant on successive studies.

The proper use of the 10 degree head downward position together with the knee-chest posture obviates the necessity of specially constructed tables or restraining devices or the aid of attendants for cervical myelography in patients who have no gross muscular disturbances. If the patient is cooperative it is possible for the roentgenoscopist to perform the examination without help and with very little discomfort to the patient. We have not achieved the same results with the knee-chest posture in the horizontal position, but others have reported better results.[4] Patients with kyphosis or scoliosis of the thoracic spine cannot be examined in this way as a rule, but myelography may be readily accomplished if the patient is placed in a lateral position.

DIAGNOSIS

The diagnosis of cervical spinal canal tumors rests on the observation of the advancing head of the pantopaque column for filling defects. These may be transient, and may assume arcuate or curvilinear configurations. A definite lesion will produce the same deformity on successive examinations, and the observer must be sure that the spinal canal is adequately visualized on either side. Inasmuch as these filling defects may occur as high cephalad as the foramen magnum, it is often impossible to prevent the passage of pantopaque into the basilar cisterns. As a rule, the oil can be returned promptly to the spinal canal by reversing the patient's position, and advantage may be taken of this procedure by observing the descent much the same as after a cisternal instillation.

REACTIONS

Thus far we have observed but two reactions which might be ascribed to the entrance of pantopaque into the basilar cisterns. The first occurred in a woman, aged forty-four, and started one week after cervical myelography, which was negative. She suddenly complained of intense vertigo which came on without warning and gradually diminished until it disappeared after four days. The second reaction occurred in a man, aged forty-six, who also had a negative cervical myelogram. He complained of intense headache which started five days after examination and gradually disappeared after two days. Lateral roentgenograms of the skulls of both patients showed droplets of pantopaque retained in the basilar cisterns.

REPORT OF CASES

Case 1 (J. H. No. 231456). H. G., male, aged twenty-nine, complained of a sharp pain starting at the tip of the right shoulder and radiating down the flexor surface of the arm to the elbow. The pain, which started four months before admission, became gradually worse and was started or aggravated by exertion or strain. There was no weakness, paresthesias or loss of manual dexterity.

Physical examination revealed slight tenderness over the middle and lower cervical spine. Neurological examination was normal.

Cerebrospinal fluid examination revealed manometric indications of a partial block. The protein content was elevated to 107 mg. per 100 cc. The Wassermann reaction and colloidal gold curve were negative.

Anteroposterior, lateral, right and left oblique stereoroentgenograms of the cervical spine showed no bony change. The intervertebral spaces were normal. Pantopaque myelography

showed free passage of the oil to the level of the interspace between the fifth and sixth cervical vertebrae, where a transitory block occurred, after which the oil slowly trickled into the axillary pouches on either side. In the cephalad end of the oil column a small hemispherical defect convex caudad was noted overlying the spinous process of the fifth cervical vertebra.

A laminectomy uncovering the fourth, fifth and sixth cervical segments revealed a soft, gelatinous yellow-white tumor about 4 cm. long lying on the dorsal aspect of the cord attached to the posterior root of the right fifth nerve. The tumor entered but did not pass through the right intervertebral foramen. It was removed completely and the patient made an uneventful recovery.

Microscopic examination revealed a perineurial fibroblastoma.

Case II (J. H. No. 277442). M. G., female, aged twenty-six, noted tingling in the second finger of her right hand, then intermittent aching pain in the right shoulder and drawing pains in the right arm for about two years before admission. After two months all the symptoms disappeared except for the tingling of the finger. A year later she noted paresthesias in her right arm, followed by twitching of both hands, numbness and increased sensitivity of both upper limbs. She began to limp on her right leg and had some difficulty in voiding for one month.

Physical examination revealed weakness of the right arm and leg, decreased tendon reflexes on the right side and diminished sensitivity to heat, cold and pin prick on the left side up to the level of the upper cervical segments.

Spinal fluid examination showed no manometric indications of block. The cerebrospinal fluid protein was elevated to 71 mg. per 100 cc. The Wassermann reaction and colloidal gold curve were negative.

Anteroposterior, lateral, right and left oblique stereoroentgenograms of the cervical spine showed no changes in the osseous or intervertebral structures. Myelography revealed a transitory, small hemispherical filling defect with the convexity directed caudad in the advancing head of the oil column on the right side at the level of the interspace between the first and second cervical vertebrae. The pantopaque entered the basilar cisterns and emerged without delay when the patient was returned to the upright position.

Laminectomy exposing the first, second and third cervical segments revealed an encapsulated intradural extramedullary tumor about 2 cm. long and 1.5 cm. thick to the right and posterior to the spinal cord. About two-thirds of the tumor lay in the spinal canal and one-third extended into the foramen magnum. The tumor was removed and the patient made an uneventful recovery.

Microscopic examination revealed a psammomatous meningioma.

Fig. 1. Case II. Spot roentgenogram revealing a small hemispherical defect in the head of the pantopaque column at the level of the interspace between the first and second cervical vertebrae. Meningioma found at operation.

Case III (J. H. No. 275513). R. N., female, aged fifty-five, first noted pain in the back of the neck about eighteen months before admission, followed by tingling in the fingers of both hands and progressive paralysis beginning in the right upper extremity, then the left upper limb followed by right lower and then left lower limb paralysis.

She had a complete tetraplegia when admitted, with her lower limbs held in a fixed flexed position. Physical examination revealed corresponding reflex changes, with complete loss of sensation to touch, pressure, pain, tem-

Fig. 2. Case III. Spot roentgenogram revealing an arcuate defect in the cephalad end of the oil column at the level of the interspace between the fifth and sixth cervical vertebrae. Meningioma found at operation.

perature, position and vibration over her entire body up to the level of the fourth cervical vertebra.

Cerebrospinal fluid manometric studies revealed a complete block. The total protein was increased to 490 mg. per 100 cc. The Wassermann reaction and colloidal gold curve were negative.

It was possible to obtain only an anteroposterior and lateral roentgenograms of her cervical spine, which were negative. Myelography, which was performed with the patient in the lateral position, revealed an almost complete block at the level of the sixth cervical vertebra, with a ribbon of oil trickling to the right of the spinal canal. At the cephalad end of the lateral ribbon overlying the right side of the interspace between the fourth and fifth cervical vertebrae there was a persistent arcuate defect concave caudad about 1 cm. wide.

Laminectomy uncovering the third to sixth cervical segments showed the spinal cord to be compressed to about one-sixth its usual size by a large intradural extramedullary tumor about 4 cm. long and 3 cm. wide. The tumor was solid, pinkish in color, homogeneous and encapsulated, and attached to the dura at one point. It was enucleated and the patient was discharged markedly improved able to move all her limbs.

Microscopic examination revealed a psammomatous meningioma.

Case IV (J. H. No. 273320). N. S., female, aged twenty-six, first noted pain in the base of her neck radiating down the right shoulder two years before admission. Numbness of the finger tips of both hands was noted one month ago, and the right arm became awkward and heavy in its movements. Transient twitchings of all four extremities was present, and she had difficulty in balancing herself on the right.

Examination showed moderate weakness of the right hand grip. Her gait was normal. The tendon reflexes were brisk, somewhat more marked on the right. The abdominal reflexes were absent, and the Hoffman and Babinski reflexes were pathologic bilaterally. There was marked stiffness of the neck, but no tenderness was elicited.

Cerebrospinal fluid examination showed normal manometric responses. The total protein was increased to 235 mg. per 100 cc. The Wassermann reaction and colloidal gold curve were normal.

Anteroposterior, lateral, right and left oblique stereoroentgenograms of the cervical spine showed no osseous or intervertebral changes. Pantopaque myelography revealed a partial block in the upper cervical spinal canal at the level of the first and second cervical vertebrae, where the head of the oil column swung from right to left and some of the oil entered the cisterna magna. A fluid level formed at the caudal end of the oil column when the patient was maintained in the inverted position. The left axillary pouch at the interspace between the second and third cervical vertebrae filled well, that on the right was not visualized.

Laminectomy of the second, third and fourth cervical vertebrae revealed a large subarachnoid extramedullary tumor extending from the top of the fourth cervical vertebra underneath the first cervical vertebra into the cranial cavity. The tumor was removed piecemeal. It was of mushroom shape, with the head extending into the cranial cavity and the stem extending alongside the spinal cord on the right occupying a lateral as well as an anteroposterior position down to the top of the fourth cervical vertebra.

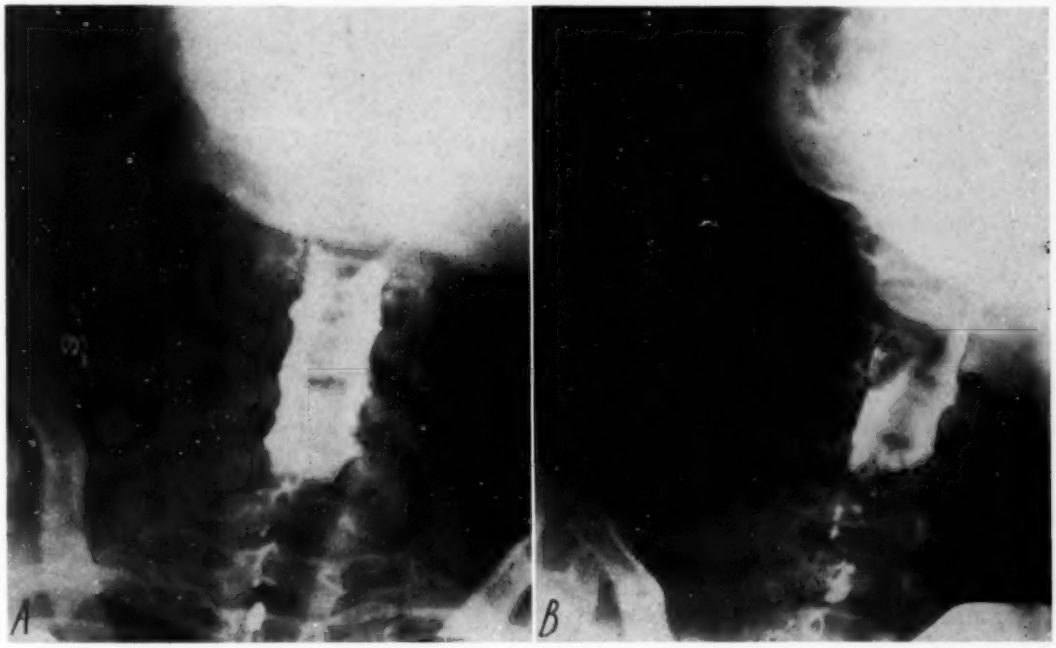

Fig. 3. Case iv. *A*, spot roentgenogram of lower cervical canal revealing normal configuration of the pantopaque column. *B*, spot roentgenogram of oil column in upper cervical spinal canal revealing filling defect on the right at the level of the upper three cervical segments. Perineurial fibroblastoma found at operation.

The tumor was yellowish, glairy, soft and friable. The patient's recovery was uneventful and she was discharged relieved of symptoms.

Microscopic examination revealed a perineurial fibroblastoma.

Case v (J. H. No. 271237). S. C., female, aged thirty-seven, first noted stiffness of her right leg about fifteen months before admission. Three months later weakness of her right hand appeared and progressed so that she was unable to hold anything. The condition improved somewhat after physiotherapy but soon recurred and was accompanied by weakness of the left hand and left leg for about three months.

Physical examination revealed active tendon reflexes bilaterally, with absent abdominal reflexes and a pathologic Babinski sign on the left side. A pathologic Hoffman sign was present bilaterally. The finer coordinated movements of the right hand were lost. There was past-pointing with both upper extremities. Impairment of temperature sensation was present in both lower limbs.

Anteroposterior, lateral, right and left oblique stereoroentgenograms of the cervical spine were normal. Myelography showed free

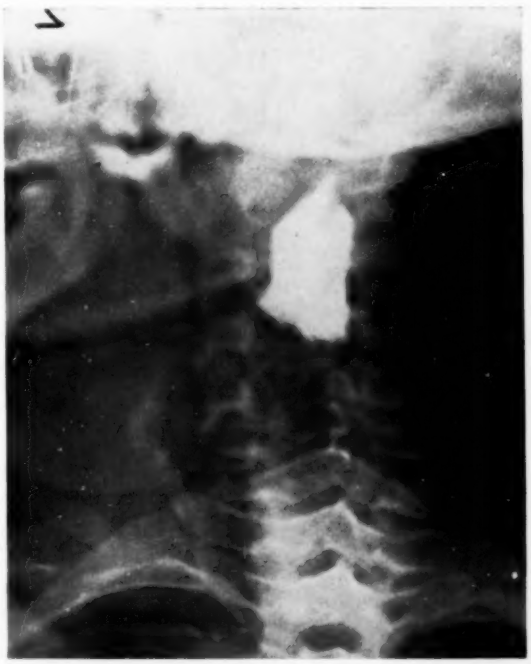

Fig. 4. Case v. Spot roentgenogram of upper cervical spinal canal revealing filling defect at level of upper two cervical vertebrae. Perineurial fibroblastoma found at operation.

passage of the oil through the lower cervical canal. The head of the oil column swerved sharply from left to right at the level of the first cervical vertebra, the caudal end forming a fluid level when the patient was kept in an inverted position.

Examination of the cerebrospinal fluid revealed manometric evidence of a complete block. The total protein was 52 mg. per 100 cc. The Wassermann reaction and colloidal gold curve were negative.

A laminectomy uncovering the upper three cervical vertebrae revealed an encapsulated extradural yellowish pink-gray tumor which was removed without difficulty. The patient made an uneventful recovery.

Microscopic examination revealed a perineurial fibroblastoma.

COMMENT

Four of the 5 patients were less than forty years old and one was fifty-five years old. The duration of symptoms was from fifteen months to two years in 4 patients, and four months in one. The onset of symptoms was insidious, and all noted pain in the back of the neck radiating to the shoulders. Four of the patients complained of pain in the right shoulder as an initial symptom, and it is conceivable that if the lesion were contralateral the pain may have simulated that encountered with coronary artery disease. Two patients had symptoms referable to the lower extremities, and 1 had a complete tetraplegia. The other 2 had no pain referable to the lower limbs.

There were 3 patients with tumors in the upper third of the cervical spinal cord, two of which extended into the cranial cavity, and two occurred in the lower third. The difference in the patterns of pain in the two groups was slight, and one could not definitely ascertain the level involved from the clinical picture alone. Thus, the first patient who had a perineurial fibroblastoma at the level of the fifth and sixth cervical vertebrae complained only of right shoulder pain with no other neurological signs, while the second patient who had a meningioma at the level of the first and second cervical vertebrae complained first of pain in the right shoulder, then of changes in sensation of both arms and the right leg and diminished perception of pin-prick on the left side. The third patient, who had a complete tetraplegia had a lesion at the level of the sixth cervical vertebra. The fourth and fifth patients both had tumors at the first and second cervical vertebral level but presented dissimilar neurologic pictures. The fourth patient complained chiefly of neck pain radiating to the right shoulder, while the fifth complained first of pain in the right leg followed by weakness and pain first in the right hand and then the left hand and leg almost a year later. Essentially the pattern presented varied with the results of the pressure produced in each individual.

The most important cerebrospinal fluid finding was elevation of the protein content. Complete cerebrospinal fluid block occurred in 2 patients, 2 had a partial block and 1 had no demonstrable block. The presence of block appeared to be more dependent on the location of the tumor than on its size in the limits mentioned here.

Three of the tumors were perineurial fibroblastomas and two were meningiomas. They had in common the important fact that they were extramedullary and could be removed completely. All the patients recovered.

Complete direct roentgenographic examination was of no help. This is not always the case, perineurial fibroblastomas being frequently diagnosed because of widening of the affected intervertebral foramen and meningiomas often presenting the end-result of pressure on the laminae and pedicles of the adjacent vertebrae. Nevertheless, it is worth repreating that in this group of patients, who had tumors for as long as two years, no direct roentgenographic evidence of pressure effects on the vertebrae could be demonstrated on complete careful direct roentgenographic examination.

SUMMARY

Pantopaque myelography fills a gap in the diagnostic procedures available for the study of the cervical spinal canal. The ease

with which it may be performed and the richness of the information available make it a most important diagnostic method. It has already achieved widespread use in the identification of herniations of the nucleus pulposus of the lower cervical spine, and, as suggested by this report, may well be extended to the study of the upper cervical region.

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THE EHLERS-DANLOS SYNDROME*

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THE Ehlers-Danlos[3,4] syndrome is an uncommon but well defined clinical entity consisting of (1) hyperelasticity and (2) fragility of the skin and blood vessels, (3) hypermobility of the joints, (4) pseudotumors over the bony prominences and (5) movable nodules beneath the skin. The disease is classified as a congenital dystrophic anomaly, but aside from the fact that it exhibits hereditary or familial tendencies,[2] little is known concerning its etiology. That the disease is probably a developmental error is supported by the frequent coexistence of additional anomalies. Synostosis of the proximal heads of the radii and ulnae,[8] club feet,[6] supernumerary teeth,[5] congenital muscular atony[12] and delayed cranial ossification[13] are some of the associated developmental faults which have been reported.

In describing the syndrome under the name cutis hyperelastica, Ormsby and Montgomery[9] state that the soft velvety skin of these patients is loosely attached to the underlying tissues and, due to an actual increase in the amount of elastic tissue, the distensibility of the skin resembles that of animals. As a result, the skin may be grasped between the thumb and forefinger and extended in a rubber-like fashion as much as 3 or 4 inches, but in contradistinction to cutis laxa, it will resume its normal position when released. This startling hyperelasticity is generalized, but is most pronounced around joints. The hyperextensibility of the joints characteristic of this condition sometimes leads to spontaneous subluxations. It is actually possible for some of these patients to touch the dorsum of the hand with the finger tips of that same hand.

The hyperelasticity of the skin is associated with extreme fragility. Slight trauma produces large gaping wounds which invariably leave rather characteristic linear or irregular papyraceous scars. Another unfortunate complication of relatively minimal injury is the formation of purplish, molluscoid pseudotumors over the various prominences of the body, particularly the elbows and knees. Skeer and Kaplan[14] explain the development of these pseudotumors on the basis of extravasation of blood into the wounds produced by trivial injury. Eventually the traumatic hematomata undergo partial absorption, leaving masses of scar tissue which can be palpated through the skin. These masses are covered by semitranslucent membranes through which their coloring, resembling that of hemangiomata, can be seen.

Ronchese[10,11] has emphasized that the four characteristic features of the symptom-complex under discussion may exist singly or in any combination, but as such cannot always be designated as the true Ehlers-Danlos syndrome. For example, many so-called "double jointed" persons have such a degree of hyperflexibility of their hands that they can subluxate interphalangeal articulations at will, although there is no associated abnormality of the skin. Hyperelasticity of the skin, either with or without excessive flexibility of joints, is an invariable finding in the "india rubber man" of side-show fame; increased skin fragility and its direct sequelae are notably lacking.

In 1934, Tobias[15] submitted the first report of the Ehlers-Danlos syndrome in the United States, calling particular attention to an apparent associated abnormality identified by him as congenital lipomatosis. The alleged lipomata manifested themselves as relatively small, firm, non-tender, subcutaneous nodules which exhibited an unusual degree of mobility. As long ago as

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1912, Shaw and Hopkins[13] had reported a patient with Ehlers-Danlos syndrome who had hard, movable subcutaneous nodules which they considered to be fibromata or neuromata. In discussing this paper, Weber told how Morris in 1900 had biopsied a similar lesion in another patient with hyperelastic skin. The nodule "seemed to consist of a spherical fibrous outer portion (in which was possibly a zone of calcification) and a fluid inner portion." Morris' patient and 2 others with similar changes were reviewed by Weber[16] in 1923. Fifteen years later, Weber and Aitken[17,18] described in great detail a patient of their own in whom they had observed subcutaneous "spherules" associated with the original Ehlers-Danlos signs.

Whereas Weber and Aitken supported the idea of Tobias that the peculiar subcutaneous nodules represent a fifth component of the syndrome in certain cases, they did not concur in his explanation of the nature of these lesions. They described the nodules as shot-like, oil-containing cysts surrounded by fibrous or calcified capsules. Presumably the nodules resulted from localized avascular degeneration of adipose tissue with subsequent repair.

It is the "fifth sign" of the Ehlers-Danlos syndrome which is of particular importance to radiologists. Our interest in the condition was kindled recently by the observation of disseminated soft tissue calcium deposits in the extremities of two sisters presenting typical clinical signs of the syndrome. This interest was intensified by a review of the literature on the subject which revealed that no roentgenograms illustrating the calcified subcutaneous nodules appear to have been published. Several reports included roentgenograms of the hands and wrists for the purpose of demonstrating hyperflexibility of the joints. In a few articles it was stated that roentgen examination of the long bones had shown no abnormality. Bolam,[1] in describing the case of a fourteen year old boy, mentioned that "on x-ray, many circular shadows could be seen and the report suggested a slight degree of calcification at these sites." No other reference to positive roentgen findings could be found.

CASE REPORTS

The roentgenographic features observed in the case of two sisters who belong in the Ehlers-Danlos category are herewith presented. A more comprehensive study including dermatological and genetic considerations will be reported elsewhere by Johnson and Falls.[7]

Case 1. V.M.E., a white girl, aged eighteen, was first seen in the Dermatological Out-Patient Department of the University Hospital on May 11, 1944, where the diagnosis of Ehlers-Danlos syndrome was made by Dr. Sture Johnson. The patient was referred to the Department of Roentgenology for examination of the spine and wrists because she complained of pain between the shoulder blades and numbness of the fingers.

The cervical and thoracic portions of the spine appeared normal. The distal end of the left radius was deformed slightly and surrounding soft tissues contained several small, rounded deposits of calcification. Additional roentgenograms of the entire left arm were requested to determine the extent of the soft tissue lesion which was thought to be a hemangioma producing bone erosion. This examination showed widespread calcium deposits extending all the way to the shoulder, and since there were no clinical signs of angioma, roentgenograms of the entire body were made to determine whether subcutaneous calcium deposits were widespread. Incidentally, while films were being exposed, the left sleeve of the patient's gown caught in the railing of the tube stand. Apparently the underlying skin was pinched slightly and although the patient complained of no pain whatsoever, a sizable wound resulted, necessitating immediate emergency care for control of bleeding.

Comment. Roentgenograms of all four extremities show striking soft tissue abnormality consisting of disseminated, small, rounded, discrete, calcareous nodules. These appear to involve either the skin itself or the immediate underlying tissues (Fig. 1). In the upper extremities these calcifications are seen to be largest and

Fig. 1. Case 1. Calcified subcutaneous lobules of fat in Ehlers-Danlos syndrome. Distribution is bilaterally symmetrical and largely superficial. Wavy irregularity of skin surface is due to traumatic hematomata (pseudotumors).

most numerous on the extensor surfaces, being particularly abundant over the lower deltoid regions (Fig. 2). A few scattered nodules are evident on the medial aspect of the upper arm, but the flexor surfaces of the forearm are entirely normal in appearance.

Involvement of the thighs is limited almost exclusively to the extreme lateral surfaces, with distribution around the greater trochanteric regions being somewhat more generalized but always superficial.

By far the greatest concentration of calcified "spherules" is present in the lower legs. Here the lesions are more widely disseminated, although a definite predilection for the lateral and medial skin surfaces is manifested. The flexor surfaces of the knees and all of the soft tissues around the ankles for some distance above the ankle joints contain none of the concretions. No nodules are found about the distal portions of the forearms, the wrists, hands, feet, scalp or trunk.

At first glance it appears that the pattern of skin calcification conforms to those portions of the extremities most subject to trauma, but this is true only where there is an appreciable amount of adipose tissue. Thus, there are numerous calcium deposits over the hips and upper arms, but the elbows, knees and ankles show little or no involvement. In direct contradistinction, the larger pseudotumors are most prominent around the joints.

Individually, the subcutaneous calcium deposits have a rather constant appearance (Fig. 2). In most instances, a central zone of relatively increased radiolucency is surrounded by a ring-like shadow of lime salt. Some of the nodules are faintly stippled and a few are entirely homogeneous, but these are in the minority.

Case II. V. E., a white girl, aged sixteen, was sent to the University Hospital Bone and Joint Department on April 20, 1944, for treatment of a tumor involving her left knee. Roentgenographic signs of primary malignant neoplasm of the proximal portion of the left tibia were

confirmed by biopsy. The tumor was an osteochondrosarcoma.

Unknown to the Department of Roentgenology, the patient was referred to Dermatology because peculiar hyperelasticity of her skin had been noted. Dr. Sture Johnson made a diagnosis of Ehlers-Danlos syndrome. When the roentgenologic signs, already described, had been observed in Case 1, the leg roentgenograms showing the bone tumor (Case 11) were reviewed

Fig. 2. Case 1. Prominent collection of nodules over left deltoid insertion. Dense outer margins and relatively radiolucent centers characterize most of the lesions.

Fig. 3. Case 11. Ehlers-Danlos syndrome. (Roentgenogram of surgical specimen. Left leg amputated because of osteochondrosarcoma, upper end of tibia.) Small calcified nodules can be seen on lateral aspect of leg.

but, because heavy exposure had been used to show bone detail, superficial tissues could not be seen clearly. Subsequent supracondylar amputation of the patient's left leg, however, afforded a splendid opportunity to scrutinize the calcified nodules more closely from both the roentgenologic and pathologic aspects.

Roentgenograms of the surgical specimen, lightly exposed, showed only a fraction of the great number of calcified subcutaneous nodules observed in the extremities of the patient's sister, but nevertheless they were of the same general configuration and distribution (Fig. 3).

Gross pathologic examination of the amputated leg (exclusive of the tibial neoplasm) showed the skin to be very hyperelastic with "peculiar scarring over the prominences." There were many subcutaneous nodules varying from the size of a millet seed to a pea, some of which were obviously calcified. Histopathologically, these concretions proved to be partially calcified lobules of subcutaneous fat (Fig. 4).

Comment. Microscopic review of the subcutaneous concretions in this patient reveals several features of considerable

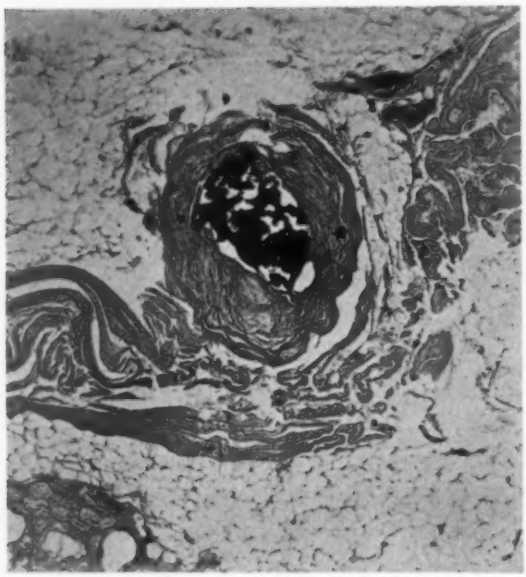

Fig. 4. Case 11. Low power microscopic section of typical subcutaneous nodule. Calcified necrotic fat (center) is surrounded by collagenous fibrous tissue capsule.

interest. Only a small percentage of the total number of nodules contain any calcium deposition whatsoever, the majority consisting of isolated groups of fat cells tightly compressed within collagenous fibrous capsules of varying thickness. A few of the fat cells have normal appearing nuclei, but for the most part they are definitely necrotic, and it is within this tissue that calcium is deposited. Occasional foreign body giant cells are seen dispersed throughout the necrotic fat. Uniform increase in elastic tissue is clearly evident in the corium.

The ring-like peripheral density observed roentgenographically in many of the larger nodules is somewhat difficult to rationalize on the basis of the microscopic findings which show the lime salt to be located centrally. It should be remembered, however, that some of the smaller nodules have a more homogeneous density and these are undoubtedly the ones from which histologic sections were made. Apparently in the case of the larger nodules, calcification is most pronounced just inside the fibrous outer capsule, with the central portion consisting largely of radiolucent non-calcified fat.

The etiology of the subcutaneous nodules in the Ehlers-Danlos syndrome is open to considerable speculation. The opposing views of Weber and Aitken, Tobias, and Shaw and Hopkins have already been mentioned and certainly additional opinions have been expressed in the past. It may well be that trauma plays more than a minor rôle in the formation of these lesions. The presence of necrotic fat and foreign body giant cells within the nodules as well as the distribution of these "spherules" on the extensor surfaces of the extremities tend to support such an explanation.

As has been suggested, the calcified nodules superficially resemble the more commonly encountered phleboliths in hemangiomata. Adding to the confusion is the fact that the entirely independent pseudotumors of the Danlos syndrome and the

Fig. 5. Calcified hemangiomatous phleboliths in forearm of two different patients. Note similarity to subcutaneous nodules in Ehlers-Danlos syndrome (Fig. 1, 2 and 3).

irregular tumor masses of sizable angiomata present much the same roentgenographic appearance. Furthermore, both entities are sometimes associated with minor alterations of normal bone architecture. Fortunately, the clinical differentiation of the two conditions is relatively simple and careful correlation of clinical and roentgen findings will avoid any serious confusion in diagnosis.

Some of the roentgenographic features of angiomatous phleboliths actually are rather distinctive and may assist materially in differentiating these vascular calcifications from the calcified Ehlers-Danlos nodules. Whereas the latter are entirely superficial in location, phleboliths are apt to be distributed throughout the deeper soft tissues. Phleboliths show more variation in size, are more irregular in outline, and contain multiple concentric strata of calcium which give the individual concretions a crystal-like appearance (Fig. 5).

The larvae of parasites such as *Cysticercus cellulosae* may calcify in the muscles of the extremities and produce roentgenologically visible shadows which are vaguely similar to those described in conjunction with the Ehlers-Danlos syndrome. Recognition of peculiarities of shape, and due attention to clinical and laboratory data aid in their proper identification.

The far more common forms of soft tissue calcification either appear as solitary lesions or occur in such an amorphous fashion that they offer no serious differential diagnostic difficulties.

SUMMARY

1. The Ehlers-Danlos syndrome is well established on the basis of clinical findings consisting of hyperelasticity and hyperfragility of the skin, hypermobility of the joints and the formation of pseudotumors, papyraceous scars and numerous subcutaneous nodules.

2. The subcutaneous nodules, confined to the extremities, may calcify and become roentgenologically visible. Two sisters who manifested these changes are presented in brief.

3. Roentgenographically, the calcified nodules may be confused with the more commonly encountered phleboliths in hemangiomata. The differentiating features of these two entities are considered.

4. Histopathologically, the Ehlers-Danlos nodules consist of lobules of calcified, necrotic fat surrounded by dense fibrous tissue capsules.

5. Repeated trauma may be an important etiologic factor.

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A QUANTITATIVE ROENTGENOGRAPHIC METHOD FOR THE DETERMINATION OF LEFT AURICULAR SIZE

NORMAL STANDARDS

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THE importance of roentgenographic evidence of enlargement of the left auricle in the diagnosis and management of rheumatic heart disease is at present generally accepted.[4,15,18,20] Indeed, Parkinson[17] and Sosman[25] have stated that the presence of an enlarged left auricle is second in significance only to the characteristic murmurs for the diagnosis of mitral valvular disease.

The roentgenographic findings in cases with a patently normal or markedly enlarged left auricle offer little difficulty. Numerous roentgen signs have been reported as aiding in the recognition of moderate or marked enlargement of this chamber.[3,7,9,11,14,24,26,32] These findings, however, are not observed in cases with only slight enlargement of the left auricle, and considerable difficulty is frequently encountered in the recognition of a minimal enlargement.[3,6,12,20,21,25] Much of this difficulty is due to the wide variation in the outline of the auricle in normal cases, and to the absence of a sharply defined difference between the appearance of the normal and minimally enlarged auricular chamber. The purpose of this paper is to demonstrate the amount of roentgenographic variation in the appearance of the left auricle in healthy individuals and to furnish quantitative standards establishing the distribution range for this normal variation. These standards, it is believed, may be of considerable value in more clearly delineating the border between the normal and slightly enlarged left auricle.

The appearance of the barium-outlined esophagus has been firmly established as one of the most accurate methods for demonstrating the left auricular contour,[6,10,14,15,19,20,32] and has been employed as the basis of this study. Determination of the size of the left auricle (without the aid of esophageal opacification) by the direct observation of changes in the cardiac silhouette[13] has not been found sufficiently accurate for the diagnosis of a minimal enlargement.

NORMAL AND ABNORMAL ANATOMY, ROENTGENOGRAPHICALLY CONSIDERED

The esophagus enters the thoracic inlet slightly to the left of the midline between the trachea and the spine. It proceeds inferiorly to the level of the fifth thoracic vertebra, where it swings to the midline and continues downward and forward in this position. At a point 2 to 3 cm. above the diaphragm it turns toward the left and descends to enter the abdomen through the esophageal hiatus.[8,20]

There are three main impressions on the opacified thoracic esophagus as seen on the oblique and lateral roentgenograms. These from above downward are (*a*) the aortic, (*b*) bronchial, and (*c*) left auricular. The aortic impression is seen constantly. It is caused by pressure of the posterior portion of the aortic arch on the left side of the esophagus. A short distance (average 0.7 cm.) below the lower end of the aortic indentation is the inconstant bronchial impression.[6,7,15,20,24,27,29] When present, it may be caused by the left main bronchus, the trachea at its bifurcation or the right main bronchus, depending upon the variation of the relationship of the tracheal bifurcation to the esophagus (Fig. 1 and 8). Just below the bronchial indentation there is normally no impression on the esophagus for a distance of 1 to 8 cm. (average 2 to 5 cm.). This portion of the esophagus is designated as the segment "alpha" (Fig. 1

and 2). The region anterior to the "alpha" segment is occupied only by connective tissue and small mediastinal lymph nodes[9,19] (Fig. 3). Immediately below the "alpha" segment the auricular impression begins and is present for a distance of 5 to 6 cm. down to a point 2 or 3 cm. above the diaphragm.

In the oblique and lateral views, the general course of the esophagus is downward and usually anterior. Less often, the esophagus may proceed downward in a truly vertical position, and infrequently, the course is downward and minimally posterior (Fig. 4). At the sites of the three main impressions, the esophagus shows local posterior bulges, but resumes its general downward and anterior direction immediately after passing the indentations. The best indicator of the general esophageal course is the direction of the "alpha" segment, located below the bronchial indentation, since there are no local impressions by adjacent viscera on this portion of the esophagus.

The angle which the posterior border of the opacified esophageal "alpha" segment makes with the vertical axis has been designated as "gamma" (Fig. 1 and 2). This angle is a measure of the direction of the "alpha" segment and therefore is an index of the general esophageal course.

At the lower end of the "alpha" segment the normal left auricular impression on the esophagus begins. The angle between a downward extension of the posterior border of the "alpha" segment and the posterior margin of the esophagus in the upper portion of the auricular impression has been designated as the angle "theta" (Fig. 1 and 2).

The anteroposterior relationship of aortic arch bulge of the esophagus to the auricular bulge varies. Usually, the aortic arch displaces the esophagus more posteriorly than does the normal left auricle. This relationship is determined as follows: From the most posterior point on the posterior border of the opacified esophageal shadow in the aortic bulge a vertical line is dropped. The distance between this line and the most posterior point on the posterior esophageal border in the region of auricular impression is determined. This distance has been designated as "*M.P.*"; i.e., maximal posteriority of the esophageal auricular bulge in relation to the aortic impression (Fig. 1, 2 and 5). The value of "*M.P.*" depends upon three major factors. These are: (*a*) the general anterior (or vertical or posterior) direction the esophagus takes as it courses downward; (*b*) the amount of local bulging in the auricular region; (*c*) the amount of local bulging in the aortic arch region.

The selection of a series of quantitative indices for the determination of the left auricular size was influenced by a consideration of the changes in the appearance and size of the left auricle in cases with definite mitral disease. It was felt that strict statistical analysis of the normal variations of the indices selected and observations on abnormal cases might be of great aid in more clearly establishing the border between the normal and enlarged auricle. A brief review of some of these considerations therefore follows.

The left auricle, as it enlarges, expands in a posterior direction early in its course.[6,9,10,15,19,20,22,25,32] Upward enlargement is usually seen shortly afterward. Enlargement to the right and left usually becomes more apparent only after the posterior expansion has been impeded by adjacent structures such as the aorta and spine. Thus, the best criteria of early enlargement appear to be posterior and upward bulging of the auricle. Since the esophagus lies adjacent the posterior wall of the left auricle, the first manifestation of enlargement should be an increase in the posterior displacement of the juxtaauricular portion of the esophagus, i.e., "*M.P.*" This posterior displacement should also be indicated, in the early phases, by an increase in the angle between the lower end of the "alpha" segment and the upper portion of the esophageal impression (i.e. the angle "theta"). With additional dilata-

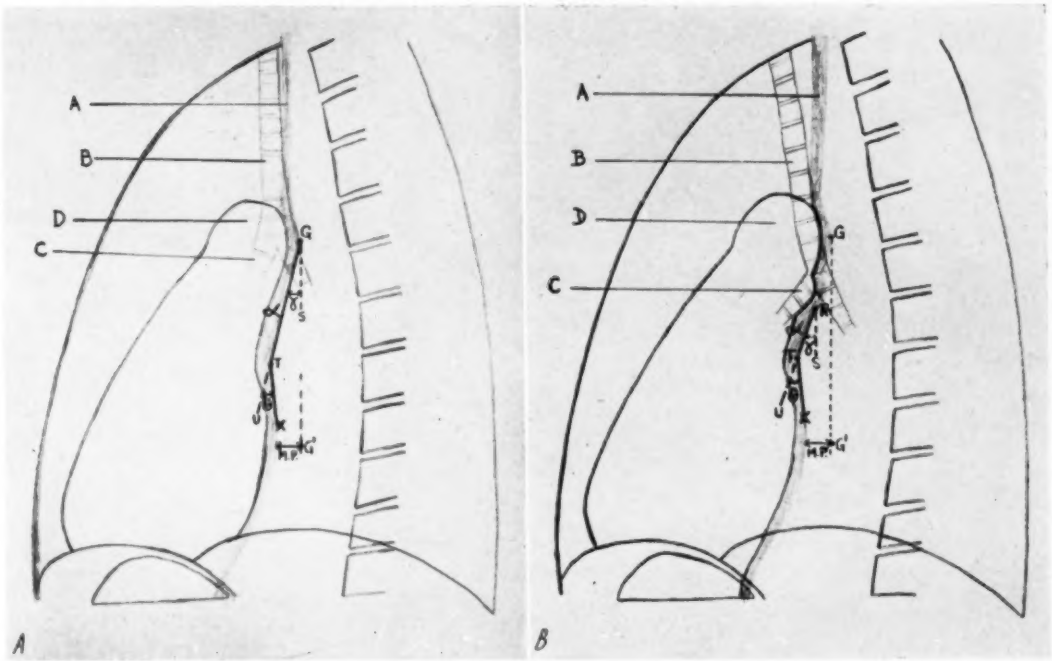

Fig. 1. Diagram of esophagus in normal case. (*A*) Shows no bronchial impression on esophagus. *A*, esophagus; *B*, trachea; *C*, left main bronchus; *D*, aortic arch; line *GT*, "alpha" segment; angle *TGS*, "gamma"; angle *UTX*, "theta"; "*M.P.*," distance from most posterior point on posterior border of esophagus in the auricular region to a vertical line (*GG'*) dropped from the most posterior point on the posterior border of the esophagus in the region of the aortic knob indentation. (*B*) Shows esophageal impression by left main bronchus. Note that in the presence of a bronchial impression the "alpha" segment (*TR*) is shortened. Angle *TRS*, "gamma." Other identifying letters are the same as in (*A*).

tion, however, the auricle expands upward as well as further posteriorly, and the lower end of the "alpha" segment is seen to become displaced backward. In these cases the entire "alpha" segment then assumes a downward and posterior course rather than the usual (in the normal) downward and anterior direction. As a result, there should be noted a diminution of the angle "theta," as well as an increase in the posteriority of "*M.P.*" and the angle "gamma." These changes actually have been found to occur before evidence of auricular enlargement to the right or left, elevation of the left main bronchus, and widening of the tracheobronchial angle appeared.

Methods were therefore employed to yield quantitative measurements for the indices of left auricular size: (1) the angle "theta," (2) "*M.P.*," and (3) the angle "gamma." A series of other measurements, namely (*a*) height and weight relationship, (*b*) frontal cardiac area, (*c*) transverse cardiac diameter and (*d*) thoracic height were also made, and statistical correlations calculated between these external, somatic factors and the three main indices.

MATERIAL AND METHODS

Two hundred and fifty healthy male soldiers between eighteen and thirty years of age were selected following a detailed history, physical and electrocardiographic examination. Any evidence even slightly suggestive of rheumatic fever, heart disease, cardiac murmur, elevated blood pressure or other abnormality caused exclusion from the study. A set of four roentgenograms was obtained for each examinee, measurements were made on these roent-

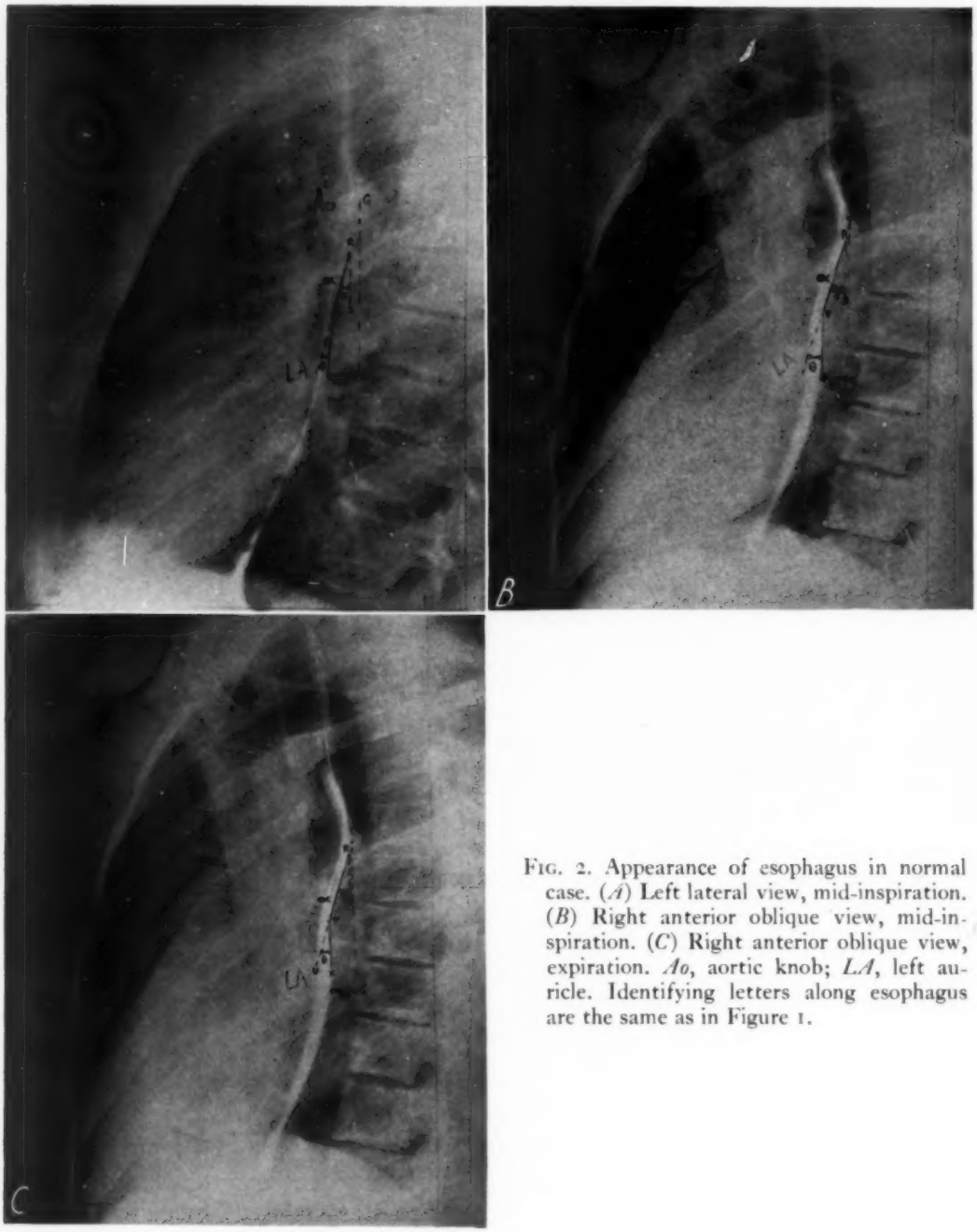

Fig. 2. Appearance of esophagus in normal case. (*A*) Left lateral view, mid-inspiration. (*B*) Right anterior oblique view, mid-inspiration. (*C*) Right anterior oblique view, expiration. *Ao*, aortic knob; *LA*, left auricle. Identifying letters along esophagus are the same as in Figure 1.

genograms, and a series of normal standards created.

The following views were employed in the study of each subject:

1. Posteroanterior in mid-inspiration.
2. Left lateral in mid-inspiration.
3. Right anterior oblique in mid-inspiration.
4. Right anterior oblique in expiration.

The esophagus was opacified for each of these views with the aid of a very thick

barium paste. The subject swallowed one mouthful, and about fifteen seconds later the exposure was made. In this manner, the esophagus was well outlined but not distended by the contrast material. Distention of the esophagus by the barium mixture was found to impair considerably the accuracy of the measurements. Therefore, the presence of a considerably distended esophagus in any view was considered as an unsatisfactory study and required re-examination. All roentgenograms were made at a 6 foot target-film distance. Correct posturing was considered essential and each roentgenogram was made with the subject standing perfectly erect. In the oblique examinations special care was required. Both shoulders of the examinee were placed evenly, eliminating any elevation on one side. Rotation of the head and neck on the thorax was avoided. A 45°–50° angle was employed, so that the shadow of the opacified esophagus cleared the spine. However, a variation from about 40° to 55° resulted in no significant discrepancies in the measurements, and no special apparatus was considered necessary for accurately establishing the degree of obliquity. In the lateral view, the arms were held above the head and the subjects stood as erectly as possible. Tendency toward slouching was corrected.

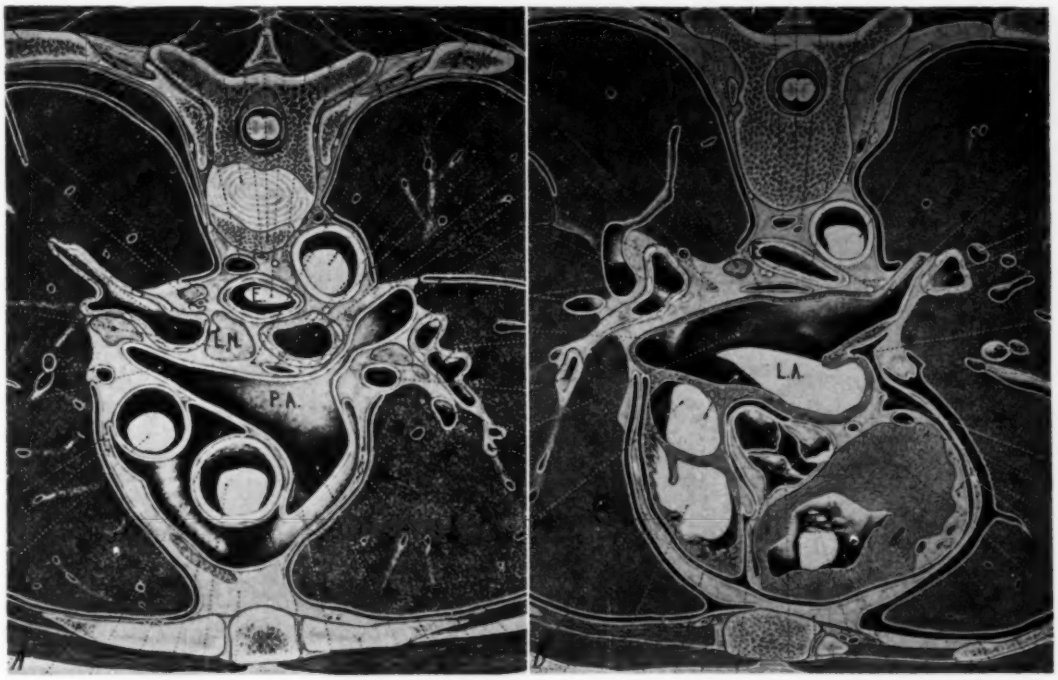

Fig. 3. Cross-section of thorax (after Eycleshymer, A. C., and Shoemaker, D. M. A Cross-Section Anatomy. Appleton & Co., N. Y., 1923, pp. 63 and 65). (*A*) Level of D_5, through "alpha" segment. Note the mediastinal lymph nodes (*L.N.*) and connective tissue between the esophagus (*E*) and the pulmonary artery (*P.A.*). The right and left main bronchi lie on each side of the mediastinal lymph nodes between the esophagus and pulmonary artery. (*B*) Level of D_7, through the upper part of the base of heart. Note the close proximity of the esophagus (*E*) to the posterior surface of the left auricle (*L.A.*).

Table 1 shows the measurements made in this study. The methods for making these measurements are as follows:

1. *Posteroanterior View.* Transverse diameter of the heart and cardiac area were measured according to the Ungerleider and Gubner[30] method. Results were recorded as percentile variations from the predicted

normal values found in the prediction tables created by these authors. Evidence of kyphoscoliosis was also noted.

2. *Both Right Anterior Oblique Views.*

(a) "*M.P.*," the maximal point of posteriority of the opacified esophagus in the region of the auricular impression as related to the esophagus at the aortic arch bulge. A vertical line is dropped from the most posterior point on the posterior surface of the outlined esophagus at the aortic impression downward to the region of the auricular impression on the esophagus. The distance between this line and the most posterior point on the posterior border of the juxta-auricular portion of the esophagus is then measured in millimeters. A "minus" sign is placed before the value when the auricular point is anterior to the vertical line dropped from the aortic bulge (Fig. 1 and 2). When the auricular point is posterior to the line of the aortic impression a "plus" sign is placed before the value (Fig. 4 and 5).

(b) Angle "theta" (Fig. 1 and 2). The apex of this angle is situated on the posterior border of the esophageal shadow at the point of junction between the lower end of the "alpha" segment and the beginning of the segment displaced posteriorly by the auricle. One limb of the angle is formed by a downward continuation of the posterior border of the "alpha" segment, the second limb by the posterior border of the upper half of the juxta-auricular segment, which approximates a straight line, or at most, forms a very shallow curve. Small local variations in the curve are to be discounted. The angle is measured with a protractor.

(c) Angle "gamma." This is the angle between the posterior border of the esophageal "alpha" segment and the vertical. It is formed by dropping a vertical line from any point on the "alpha" segment, since the value of "gamma" will be the same for any series of verticals dropped from any series of points on the segment. A point should be chosen where the posterior esophageal border is most clearly visualized and best represents the course of the "alpha" segment. The vertical limb may be obtained by drawing a line parallel with the long edge of the 14 by 17 inch film, or perpendicular to the short edge. The angle is measured with a protractor. In cases where the downward course of the "alpha" segment is anterior to the vertical line a "minus" sign is placed before the value of the angle (Fig. 1 and 2). Where the "alpha" segment proceeds downward posterior to the vertical line a "plus" sign is placed before the value of the angle (Fig. 5).

(d) Thoracic height. This is taken as the distance between the highest level of the diaphragm (right or left) and the inferior margin of the left first rib posteriorly adjacent the spine. The measurement is made in centimeters.

Table 1

MEASUREMENTS DETERMINED FROM EACH ROENTGENOGRAM

	Posteroanterior View Mid-Inspiration	Left Ventral View Mid-Inspiration	Right Anterior Oblique View Mid-Inspiration	Right Anterior Oblique View Expiration
"M. P."		×	×	×
Angle "theta"		×	×	×
Angle "gamma"		×	×	×
Thoracic height			×	×
Transverse cardiac diameter	×			
Frontal cardiac area	×			

3. *Left Lateral View.*

(a) The angles "theta" and "gamma" and the distance "*M.P.*" are measured in the same manner as in the oblique examinations (Fig. 2).

(b) Thoracic height is not measured in this view since the upper ribs cannot be clearly delineated.

4. *Other Measurements.*

(a) The height and weight of each subject are obtained and compared to a standard chart[31] to determine the variation from the average of each subject's weight for his height; i.e., habitus.

(b) The age of each subject is recorded.

Two simple measuring aids (Fig. 6) have been found extremely useful. These are: (1) A transparent protractor with a movable arm extending from its center outward over the graduated arc of its periphery. With it, the angles may be measured directly and quickly from the roentgenogram. (2) A cleared, transparent 14 by 17 inch film on which vertical lines parallel to the long side and 1 cm. apart have been accurately etched. This transparency is carefully inserted and cemented into a rigid frame so that the lines are absolutely parallel with the long axis of the frame. The film in its frame is then set on a view box (best lying horizontal) and the heart roentgenogram being studied is placed over the transparency so that the entire long side of the heart roentgenogram is in closest apposition with the frame. As a result, a series of vertical lines 1 cm. apart are superimposed upon the heart roentgenogram, and all measurements requiring the use of these lines are greatly facilitated.

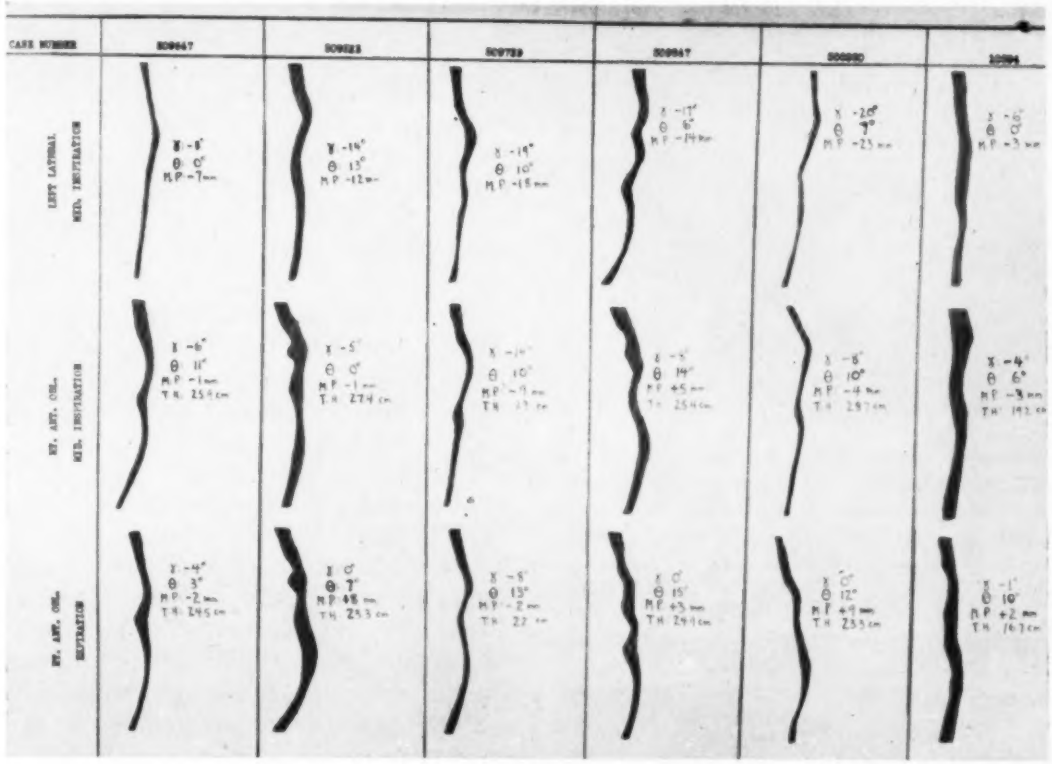

Fig. 4. Diagrams illustrating variations in the appearance of the esophagus in 6 normal cases. The index measurements are presented by the side of each drawing. The measurements for "*M.P.*" are those prior to correction.

TABLE II

INTERCORRELATIONS*

	"M. P."	"Gamma"	"Theta"
Left Lateral View, Mid-Inspiration			
Thoracic height	−.17**	—	—
Transverse diameter	−.01	−.08	.10
Frontal area	−.03	−.08	.00
Habitus	.15	.03	.12
"M. P."	—	.68	.07
"Gamma"	.68	—	−.28
"Theta"	.07	−.28	—
Right Anterior Oblique View, Mid-Inspiration			
Thoracic height	−.23	−.14	−.17
Transverse diameter	.09	.07	.16
Frontal area	.09	.04	.02
Habitus	.06	.00	.15
"M. P."	—	.74	.03
"Gamma"	.74	—	.18
"Theta"	.03	−.18	—
Right Anterior Oblique View, Expiration			
Thoracic height	−.38	−.21	−.22
Transverse diameter	.18	.05	.13
Frontal area	.14	.08	.10
Habitus	.18	.03	.15
"M. P."	—	.71	.22
"Gamma"	.71	—	−.24
"Theta"	.22	−.24	—

* The number in each box represents the correlation coefficient (r) between the two variables correlated. The 1% level of significance for $r = .16$. The 5% level of significance for $r = .12$.

** Since thoracic height could not be measured accurately in this view, the value shown represents the correlation coefficient between "*M.P.*" and the thoracic height measured on the right anterior oblique roentgenogram made during mid-inspiration.

STATISTICAL ANALYSIS AND RESULTS

The three important indices for determining the size of the left auricle were "gamma," "theta" and "*M.P.*" However, it was recognized that each of these three indices might be affected not only by the size of the left auricle but also by extra-auricular factors. In order to utilize the indices as accurate indicators of auricular size, any considerable influence on the measurements by extra-auricular causes (i.e. thoracic height, examinee's weight, height, etc.) had to be eliminated. Therefore, a series of intercorrelation analyses was made between each of the three indices, and between them and all possible extra-auricular factors in each of the three views. The Pearson Product-Moment* correlation method[2] was employed, and the coefficient of correlation of the three indices to each other and to each of the independent extra-auricular variables in the 250 normal controls was calculated (Table II). Where the correlations were small (i.e., below the 1 per cent level of significance), the extra-auricular factors were considered as not affecting the indices' measurements of left auricular size and were disregarded. On the other hand, where the correlation coefficients were large, the extrinsic factors obviously would influence the measurements and impair the indices' accuracy as indicators of auricular size. In these instances, the measurements were corrected according to the multiple, linear regression technique,[1] and the effect of the extra-auricular factors was eliminated. Following this necessary adjustment, the values could be considered accurate indicators of the size of the left auricle. The final, accurate values for "gamma," "theta" and "*M.P.*" were then arranged in frequency distributions according to magnitude and percentile tables constructed (Table VI). These

* The formula for Pearson-Moment Method is: $r_{xy} = \Sigma_{xy}/\sigma_x\sigma_y N$

Where

r_{xy} = coefficient of correlation between x and y

N = number of cases

x = deviation of the raw score, x, from mean of X

y = deviation of raw score, y, from mean of Y

σ_x = standard deviation of X

σ_y = standard deviation of Y

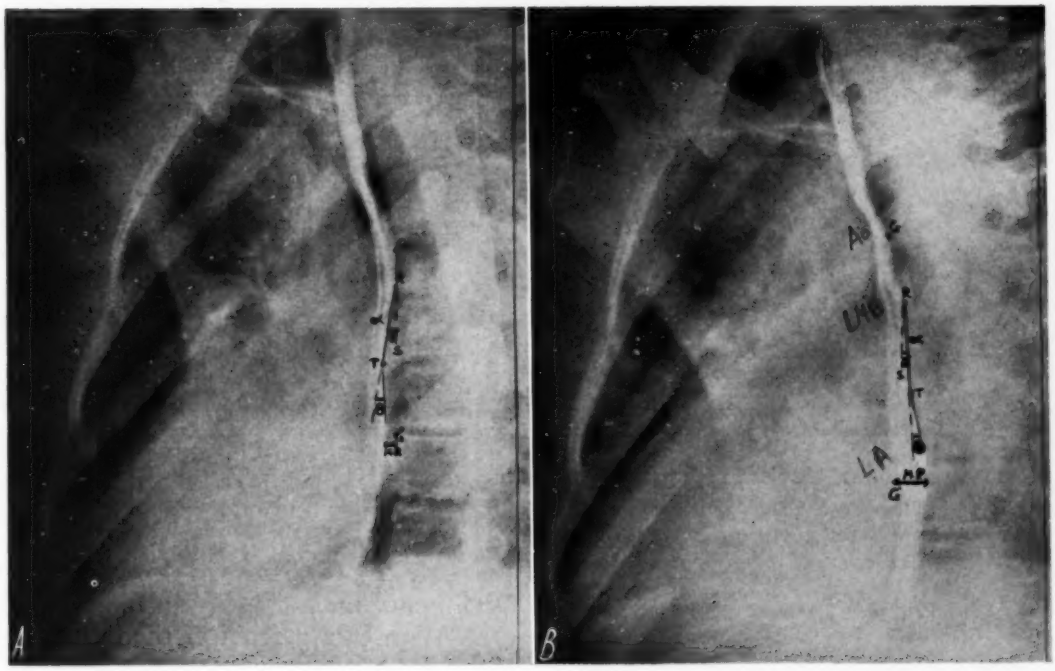

FIG. 5. The effect of marked diminution of thoracic height due to expiration on the index measurements. (*A*) Right anterior oblique view, mid-inspiration. (*B*) Right anterior oblique view, expiration. Note that the elevation of the diaphragm has caused "*M.P.*" and "gamma" values to change from negative to positive in sign; i.e., the auricular impression has become posterior to the line of the aortic impression. "Theta" is diminished in value. The esophageal shadow has been intensified to enhance its photographic demonstration. Identifying symbols are the same as in Figure 1.

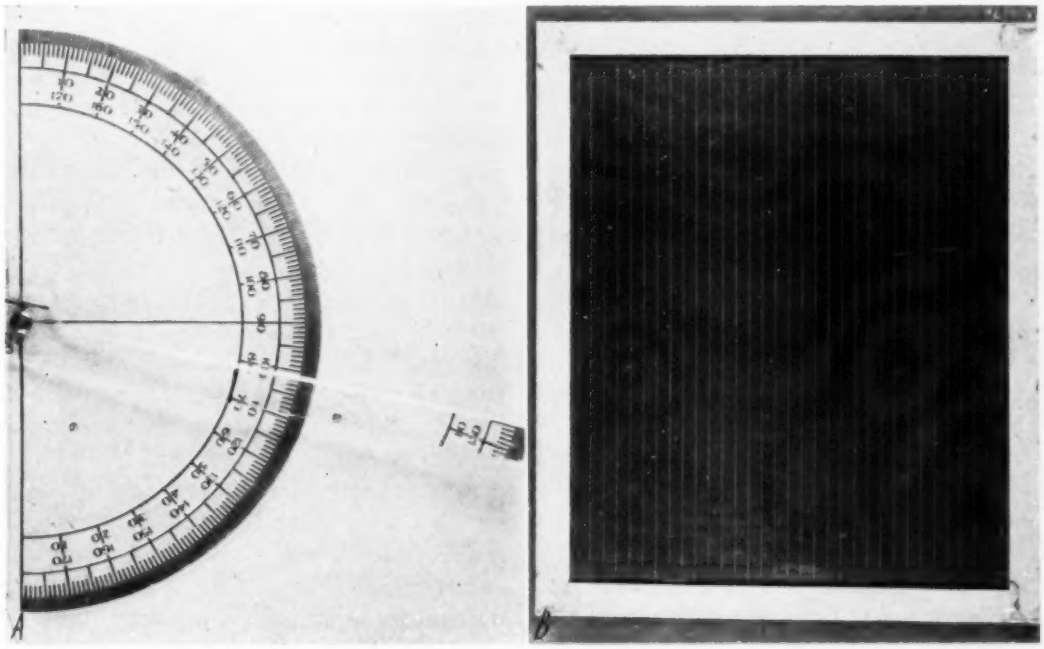

FIG. 6. (*A*) Transparent protractor used for measuring angles. (*B*) Transparent 14 by 17 inch film fixed in metal frame. Note the etched vertical lines in the film, 1 cm. apart and parallel to the long side of the frame.

percentile tables were the "normal standards" for use in evaluating the measurements obtained in a suspected case. The percentile tables indicate what percentage of the normal controls have values smaller (or greater) than those found in the case under observation.

It can be seen from Table II that there are no high correlation coefficients, requiring adjustment, between extra-auricular factors and "theta." In the left lateral and in the right oblique expiratory views the "gamma"-"theta" correlations are −0.28 and −0.24 respectively. While these coefficients are slightly higher than the 1 per cent level of significance, the calculated corrections of the value for "theta" with variations of "gamma" are of such small magnitude that they can be neglected for the sake of simplicity without significantly altering the accuracy of the final "theta" reading. Similarly, the correlation coefficients between "theta" and thoracic height and "*M.P.*" also indicate that adjustment is unnecessary. Thus, the measurements for "theta," as obtained from the roentgenograms, are to be employed without correction for percentile evaluation.

The intercorrelation table demonstrates that "gamma" also is unaffected by all extracardiac factors, and therefore the "gamma" measurements may be directly applied to the percentile tables. The high correlation between "gamma" and "*M.P.*" obviously requires correction. However, in the healthy individual the angle "gamma" actually represents the general course of the esophagus and is unaffected by normal variations in auricular size. Therefore, in the normal cases, "gamma" must be considered an extra-auricular factor and is to be employed for corrections of "*M.P.*" in establishing the normal standards. In contradistinction, the "*M.P.*" measurement, being based upon the position of the juxta-auricular segment, is greatly influenced by the normal variations of auricular size. Since "*M.P.*" measurements reflect changes of auricular size in both normal and abnormal cases, "*M.P.*" can never be considered as an extra-auricular factor and is not to be employed for corrections of "gamma" in the normal standards.

The measurements for "*M.P.*" are the only ones requiring corrections before evaluation on the percentile tables. From Table II it is apparent that "gamma," an extra-auricular factor in the healthy individual, greatly affects the value of "*M.P.*" Therefore, for the normal standards, the measured "*M.P.*" is adjusted for variations in the size of "gamma" according to their linear regression relationship. However, the interrelationship between "gamma" and "*M.P.*" is complex in that "gamma" represents more than the general direction of the esophagus in the abnormal case. With enlargement of the left auricle, the "alpha" segment is displaced posteriorly and the normal values of "gamma" change to measurements of increasing positivity. These changes in the magnitude of "gamma" obviously do not represent an extra-auricular influence, but are due directly to the auricular enlargement. Because of this, "*M.P.*" cannot be corrected for abnormal values of "gamma." Thus, corrections of "*M.P.*" for variations of "gamma" are made only to the upper limits of normal "gamma" values. Approximately the 95th percentile value of "gamma" (i.e., the value for "gamma" which is greater than that found in 95 per cent of the normal controls) has been considered as the upper limit of normal. In cases where the measured magnitude of "gamma" is greater (on the positive side) than this value, the "*M.P.*" correction for "gamma" is made only to the extent of the latter's 95th percentile value.

It is possible that corrections of "*M.P.*" for "gamma" variations may be slightly inadequate in cases of minimal auricular enlargement in which an original very low percentile "gamma" value may have been elevated into the high normal range by the dilating left auricle prior to the initial examination. The measured "*M.P.*" would then be corrected to a lesser extent since

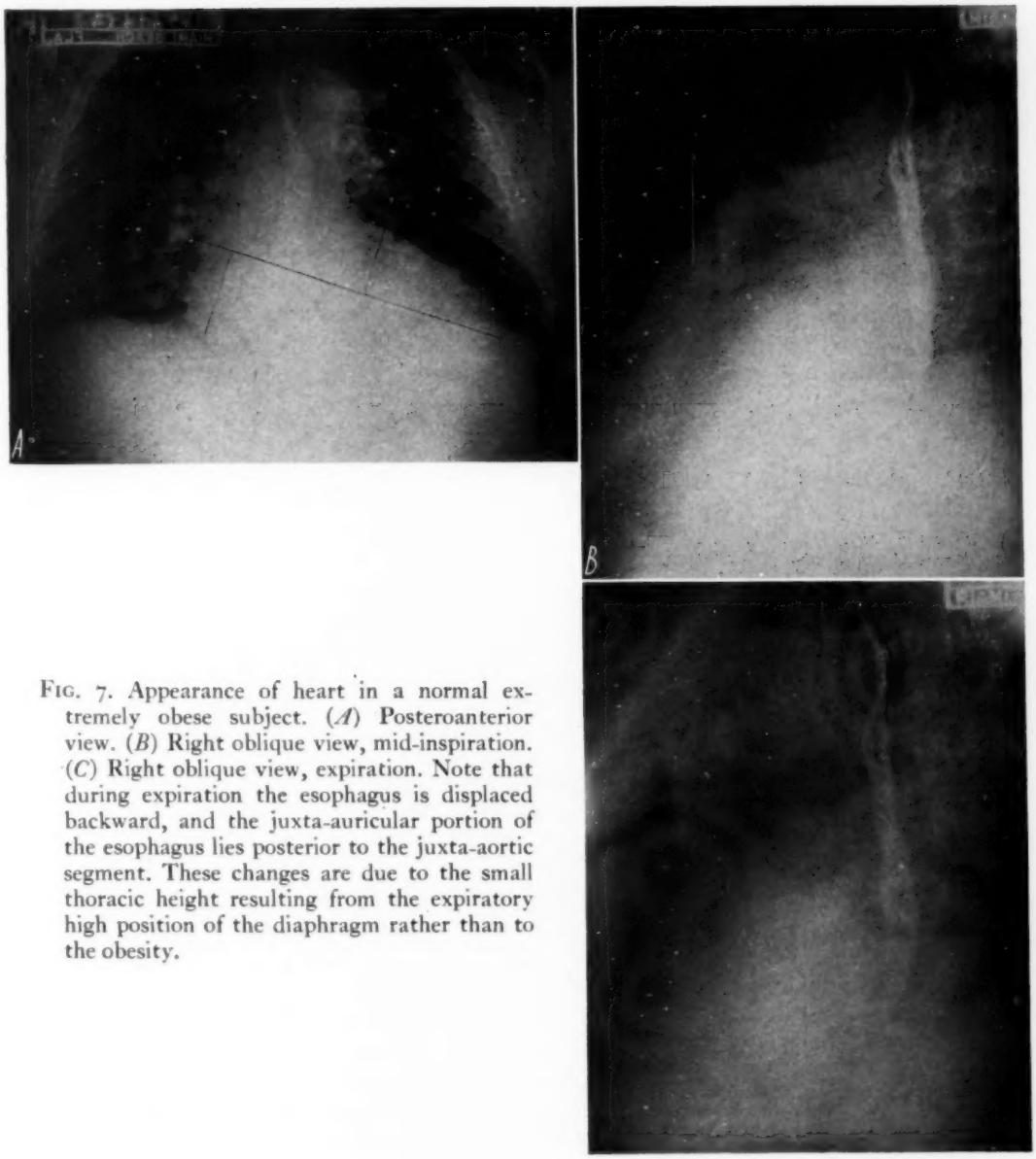

Fig. 7. Appearance of heart in a normal extremely obese subject. (*A*) Posteroanterior view. (*B*) Right oblique view, mid-inspiration. (*C*) Right oblique view, expiration. Note that during expiration the esophagus is displaced backward, and the juxta-auricular portion of the esophagus lies posterior to the juxta-aortic segment. These changes are due to the small thoracic height resulting from the expiratory high position of the diaphragm rather than to the obesity.

the assumed normal value for "gamma" would be more positive than the original "gamma" measurement. As a result, the final, adjusted "*M.P.*" measurement would be slightly less positive (posterior) than if the full correction for "gamma" (were it known) had been employed. However, this somewhat conservative procedure appears warranted. Experience thus far has indicated that posterior and upward enlargements of the left auricle, even though mild, usually increase the "gamma" value beyond the normal percentile limits. In addition, the "*M.P.*" measurements under these conditions are usually of sufficient magnitude to be considered at least suspicious. Thus, very little, if any, of the earliest left auricular enlargement is completely unrecognized.

The necessity for great care in the actual

TABLE III

CORRECTION TABLE FOR "M. P."*—LEFT LATERAL VIEW

"Gamma" Measurement**	Correction Factor to be Algebraically Added to the Measured "M. P."
0	2
− 1	3
− 2	3
− 3	4
− 4	5
− 5	6
− 6	7
− 7	8
− 8	9
− 9	10
−10	11
−11	11
−12	12
−13	13
−14	14
−15	15
−16	16
−17	17
−18	18
−19	18
−20	19
−21	20
−22	21
−23	22
−24	23
−25	24
−26	25
−27	25
−28	26
−29	27
−30	28

* The correction table is based on the following linear regression equation: Correction factor = −0.880 "gamma" +1.709.

** No additional correction is to be made for values of "gamma" above 0. For all positive values of "gamma" use the 0 correction factor in adjusting "*M.P.*"

measurement of the "gamma" angle is apparent, since the "*M.P.*" corrections are based on the correlation coefficients in the multiple regression formula. The correlation coefficient between "gamma" and "*M.P.*" is extremely high, and considerable inaccuracies in the "gamma" measurement would result in almost as great errors for the corrected "*M.P.*"

Table II shows that the intercorrelation between thoracic height and "*M.P.*" in the right oblique expiratory film (−0.38) also is of sufficient magnitude to require a correction of "*M.P.*" for variations in thoracic height (Fig. 7). The correlation coefficient between thoracic height and "*M.P.*" in the right oblique inspiratory roentgenogram is only −0.23. However, since corrections for thoracic height are made in the expiratory roentgenogram, "*M.P.*" also has been corrected for thoracic height variations in the inspiratory right oblique views. The amount of correction in the inspiratory right oblique view is, of course, much less than the correction for thoracic height in the expiratory roentgenogram. Thoracic height could not be accurately determined in the left lateral view because the first rib is not clearly visualized. However, "*M.P.*" in the left lateral view (taken at mid-inspiration) has been correlated with the thoracic height of the right oblique mid-inspiratory roentgenogram. This correlation is found to be −0.17, insufficient to require a correction.

The magnitude of the corrections for "*M.P.*" are calculated according to the multiple linear regression equation, and correction tables prepared for each of the three views. In both oblique studies simultaneous corrections are made for thoracic height and "gamma." In the left lateral view only the correction for "gamma" is required. The tables are employed as follows: In each of the oblique views (Tables IV and V) the measured values for "gamma" and thoracic height are followed along their respective rows and columns to where they intersect. The value at the intersection point is algebraically added to the measured reading for "*M.P.*" and the result is the corrected "*M.P.*" The correction table for the left lateral view (Table III) indicates the magnitude of the correction to be algebraically added to the measured "*M.P.*" for each value of "gamma."

A study of the correction and percentile tables shows that the final corrected value of "*M.P.*" is a measure of its deviation from the mean value of "*M.P.*" in the

normal controls. An individual with mean values for "gamma," thoracic height and measured "*M.P.*" would have a mean correction, and the final adjusted value for "*M.P.*" would be 0. Thus, corrected values of "*M.P.*" which are negative in sign are located below the 50th percentile,* while corrected "*M.P.*" values which are positive lie above the 50th percentile.

The final possible extra-auricular factor affecting "*M.P.*" is an abnormality of the aortic arch resulting in displacement of the juxta-aortic portion of the esophagus. Observations on the healthy controls indicate that unless the aortic arch is grossly abnormal in size, shape or position, the aortic knob maintains an essentially constant position in the upper chest, does not influence the "*M.P.*" measurement and may therefore be disregarded.

With the values for "theta" and "gamma" obtained directly from the roentgenograms and the adjusted values for "*M.P.*" from the correction tables, a percentile table is constructed for each of these three indices in each of the three views (Table VI). Each table is made by arranging the 250 measurements in a frequency distribution of ascending magnitude and

TABLE IV

CORRECTION TABLE FOR "M. P."*—RIGHT ANTERIOR OBLIQUE VIEW; MID-INSPIRATION

(Combined Thoracic Height and "Gamma" Correction Factor to be Algebraically Added to the Measured "M. P.")

	Thoracic Height in millimeters												
"Gamma" Measurement**	160 169	170 179	180 189	190 199	200 209	210 219	220 229	230 239	240 249	250 259	260 269	270 279	280 289
0	−4	−4	−4	−3	−3	−3	−2	−2	−2	−1	−1	−1	0
− 1	−4	−3	−3	−3	−2	−2	−2	−1	−1	−1	0	0	0
− 2	−3	−3	−2	−2	−2	−1	−1	−1	0	0	0	1	1
− 3	−2	−2	−2	−1	−1	−1	0	0	0	1	1	1	2
− 4	−1	−1	−1	0	0	0	0	1	1	1	2	2	2
− 5	−1	0	0	0	1	1	1	2	2	2	3	3	3
− 6	0	0	1	1	1	2	2	2	3	3	3	4	4
− 7	1	1	1	2	2	2	3	3	3	4	4	4	5
− 8	1	2	2	2	3	3	3	4	4	4	5	5	5
− 9	2	3	3	3	4	4	4	5	5	5	6	6	6
−10	3	3	4	4	4	5	5	5	6	6	6	7	7
−11	4	4	4	5	5	5	6	6	6	7	7	7	8
−12	4	5	5	5	6	6	6	7	7	7	8	8	8
−13	5	5	6	6	6	7	7	7	8	8	8	9	9
−14	6	6	7	7	7	8	8	8	9	9	9	10	10
−15	7	7	7	8	8	8	9	9	9	10	10	10	11
−16	7	8	8	8	9	9	9	10	10	10	11	11	11
−17	8	8	9	9	9	10	10	10	11	11	11	12	12
−18	9	9	9	10	10	10	11	11	11	12	12	12	13
−19	10	10	10	11	11	11	12	12	12	13	13	13	14
−20	10	11	11	11	12	12	12	13	13	13	14	14	14
−21	11	11	12	12	12	13	13	13	14	14	14	15	15

* The correction table is based on the following linear regression equation:
Correction factor = −0.737 "gamma" +0.033 thoracic height −9.858.

** No additional correction is to be made for values of "gamma" above 0. For all positive values of "gamma" 'use the 0 correction factor in adjusting "M.P."

* The 50th percentile is actually the median, and not the mean. However, the values for the median and mean are very nearly the same, and a slight change of the constant in the multiple linear regression equation allows the 50th percentile of the corrected "*M.P.*" to be placed at 0 without in any manner impairing the accuracy or value of the correction tables.

TABLE V

CORRECTION TABLE FOR "M. P."*—RIGHT ANTERIOR OBLIQUE VIEW; EXPIRATION

(Combined Thoracic Height and "Gamma" Correction Factor to be Algebraically Added to the Measured "M. P.")

	Thoracic Height in Millimeters											
"Gamma" Measurement**	160 169	170 179	180 189	190 199	200 209	210 219	220 229	230 239	240 249	250 259	260 269	270 279
2	−7	−7	−6	−5	−5	−4	−4	−3	−2	−2	−1	0
1	−7	−6	−5	−5	−4	−4	−3	−2	−2	−1	0	0
0	−6	−5	−5	−4	−4	−3	−2	−2	−1	0	0	1
− 1	−5	−5	−4	−4	−3	−2	−2	−1	0	0	1	2
− 2	−5	−4	−4	−3	−2	−2	−1	0	0	1	2	2
− 3	−4	−4	−3	−2	−2	−1	0	0	1	2	2	3
− 4	−4	−3	−2	−2	−1	0	0	1	2	2	3	3
− 5	−3	−2	−2	−1	0	0	1	2	2	3	3	4
− 6	−2	−2	−1	0	0	1	2	2	3	3	4	5
− 7	−2	−1	0	0	1	2	2	3	3	4	5	5
− 8	−1	0	0	1	2	2	3	3	4	5	5	6
− 9	0	0	1	2	2	3	3	4	5	5	6	7
−10	0	1	2	2	3	3	4	5	5	6	7	7
−11	1	2	2	3	3	4	5	5	6	7	7	8
−12	2	2	3	3	4	5	5	6	7	7	8	9
−13	2	3	3	4	5	5	6	7	7	8	9	9
−14	3	3	4	5	5	6	7	7	8	9	9	10
−15	3	4	5	5	6	7	7	8	9	9	10	10
−16	4	5	5	6	7	7	8	9	9	10	10	11
−17	5	5	6	7	7	8	9	9	10	10	11	12
−18	5	6	7	7	8	9	9	10	10	11	12	12
−19	6	7	7	8	9	9	10	10	11	12	12	13
−20	7	7	8	9	9	10	10	11	12	12	13	14
−21	7	8	9	9	10	10	11	12	12	13	14	14
−22	8	9	9	10	10	11	12	12	13	14	14	15
−23	9	9	10	10	11	12	12	13	14	14	15	16
−24	9	10	10	11	12	12	13	14	14	15	16	16
−25	10	10	11	12	12	13	14	14	15	16	16	17
−26	10	11	12	12	13	14	14	15	16	16	17	17

* The correction table is based on the following linear regression equation:

Correction factor = −0.636 "gamma" +0.064 thoracic height −16.650

** No additional correction is to be made for values of "gamma" above 2. For all values above 2, use the 2 correction factor in adjusting "M.P."

determining the values of the 10th percentile, 20th percentile, etc., up to the 99.5th percentile. Thus, the measurement in any individual case can be compared with those in the percentile chart to determine the percentage of the normal controls which have values of smaller (or greater) magnitude. Calculations demonstrate that the standard error of the percentiles is small and that the percentile distribution determinations are of sufficient statistical significance to be clinically accurate.

The percentile table arrangement of the data is considered more satisfactory than direct employment of the prediction formulae for the purposes of this study. It is felt that the percentiles are easier to use, considerably simpler to evaluate, and permit more rapid handling.

CLINICAL APPLICATION

Measurements are made as described under Method. The measurements for "theta" and "gamma" are evaluated di-

rectly from the percentile tables and the percentile value for each of these indices is recorded for the three views.* The roentgenogram measurements for "*M.P.*" are adjusted on the correction tables by algebraically adding the correction factors derived from the values of "gamma"

Table VI

TABLE OF PERCENTILES FOR LEFT AURICULAR SIZE INDICES

	Left Lateral View Mid-Inspiration			Right Anterior Oblique View Mid-Inspiration			Right Anterior Oblique View Expiration		
	"Theta"	"Gamma"	"M. P." Adjusted	"Theta"	"Gamma"	"M. P." Adjusted	"Theta"	"Gamma"	"M. P." Adjusted
Mean	5.380°	−14.108°	0.076 mm.	6.544°	−8.308°	0.088 mm.	8.944°	−5.752°	0.276 mm.
Standard Deviation	4.785°	5.576°	5.188 mm.	4.860°	5.253°	3.594 mm.	5.931°	5.623°	3.572 mm.
Percentile									
0	0	−30	−14	0	−22	−10	0	−28	−10
10	0	−24	− 7	1	−15	− 4	1	−13	− 4
20	1	−21	− 4	2	−12	− 3	2	−11	− 3
30	2	−17	− 2	3	−11	− 2	5	− 9	− 2
40	2	−16	− 1	5	−10	− 1	7	− 7	− 1
50	4	−14	0	6	− 9	0	9	− 6	0
60	6	−13	1	8	− 7	1	11	− 4	1
70	8	−11	3	9	− 6	2	12	− 2	2
80	10	−10	4	11	− 4	3	14	0	3
90	12	− 7	5	13	− 1	5	17	2	5
95	14	− 5	8	15	1	6	19	2	6
96	15	− 4	8	16	2	7	20	4	7
97	16	− 4	8	17	3	7	21	6	7
98	17	− 2	10	18	4	8	22	7	8
99	18	1	12	20	5	9	23	9	9
99.5	20	2	14	20	8	10	26	11	9

Measurements for "theta" and "gamma" are evaluated without correction. The measurements for "M.P." must be adjusted according to the correction tables before percentile evaluation is made.

and thoracic height. The adjusted "*M.P.*'s are then also evaluated on the percentile tables to indicate what percentage of the normal controls have measurements which are smaller than those obtained in the case being examined.

In the interpretation of the final percentile results for each of the indices, several factors must be considered. The diagnosis of marked enlargement or absolute normalcy of the left auricle offers comparatively little difficulty. Indeed, in these instances the findings are so obvious that qualitative evaluation is comparatively simple and accurate. However, the diagnosis becomes much more uncertain in cases where minimal enlargement and upper limits of normal size must be differentiated. What may be a normal auricular silhouette for one individual may represent minimal enlargement for another. Qualitative handling of such a status almost invariably leads to personal impressions, subjective approach and considerable confusion. On the other hand, proper quantitative analysis appears of great aid in eliminating the subjective element and in establishing a more objective basis for interpretation. The rational approach to these borderline situations, therefore, should not be a defi-

* A simple record chart for the measurements can be mimeographed and greatly expedites recording the data. Such a chart is shown in Table VII. Clinical details of the case may be entered on the reverse side.

nite declaration of normality or abnormality, frequently inaccurate. Instead, a statement should be made as to what percentage of normal controls have measurements smaller than those found in the suspected case. The interpretation of this objective, percentile finding may vary. Thus, if a suspected case has values which are greater than those found in 95 per cent of normal controls, and in addition has an apical murmur and/or gives a history of previous rheumatic fever, it may reasonably be stated that there is an extremely high probability that slight auricular enlargement exists. A situation may occur, however, in which the auricular indices also may be in the 95th percentile, but the patient shows no evidence of a cardiac murmur, gives no rheumatic history, etc. In such an instance, the same percentile value would have a distinctly different evaluation. While the size of the auricle again is greater than those in 95 per cent of normal controls, nevertheless, it is realized that 5 per cent of the controls do have values as large or larger, and the examinee may be in this upper normal group. However, reexamination is indicated. If, at the end of the follow-up period additional studies showed no increase in the percentile rating or other cardiac abnormalities, then it would appear reasonable to assume that the findings were not indicative of auricular enlargement. In cases where the auricular indices are below the 60th percentile, auricular enlargement can be excluded, despite the presence of cardiac murmurs and/or a positive rheumatic fever history. With such an attitude, a highly desirable liaison can be established between clinician and roentgenologist for the benefit of the patient, without the roentgenographic observations being influenced by the clinical findings.

In general, under the guidance of the principles mentioned above, it may be said with reasonable statistical certainty that values up to the 90th percentile are prob-

Table VII

MEASUREMENTS FOR ENLARGEMENT OF LEFT AURICLE

Name		Case No.				X-Ray No.	
	PA	Left Lateral Mid-Inspiration		Right Anterior Oblique Mid-Inspiration		Right Anterior Oblique Expiration	
		Value	Percentile	Value	Percentile	Value	Percentile
"Theta"							
"Gamma"							
Thoracic height							
"M. P." Observed							
Corrected							
Transverse Diameter Observed							
Predicted							

Height: Weight: Age:

ably normal, those between the 90th and 95th percentile suspicious, between the 95th and 100th percentile highly suspicious, and measurements above the 100th percentile are abnormal. Several roentgenographic views should be taken, since one view may show the abnormality better than another, and the percentile readings may frequently vary in the different roentgenograms of the same case. Right anterior oblique roentgenograms are made during both inspiration and expiration in an attempt to better demonstrate very early enlargement. During expiration the diaphragms rise and thoracic height becomes diminished. The heart is flattened from above downward, and the inferior portion of the heart moves backward to a slight degree. As a result, the juxta-auricular portion of the esophagus is displaced somewhat more posteriorly than during inspiration.[6,16,32] Thus, any tendency toward posterior displacement of the juxta-auricular esophagus by the left auricle is accentuated during expiration (Fig. 5 and 7), and the expiratory roentgenogram is a somewhat more delicate indicator of early auricular enlargement.[25] However, because the expiratory view is more delicate an indicator, care is required in its interpretation in order to avoid the pitfall of "false positives"; i.e., mistaking normal appearances for slight auricular enlargement.[20] The possibility of this error is minimized by the use of the percentiles, which clearly defines the position of the juxta-auricular esophagus during expiration in the normal controls. Experience thus far has indicated that in minimal enlargement of the left auricle abnormal measurements may be found only in the expiratory roentgenogram. In cases which have progressed sufficiently to become evident in the inspiratory roentgenogram, the changes are practically always more marked in the roentgenogram made during expiration.

The quantitative analysis method has not only been found of great aid in establishing the diagnosis of slight left auricular enlargement, but, in addition is also of considerable value in following patients where the diagnosis has been made from the initial examination. In these cases, increased percentile values in successive examinations has clearly indicated progressive auricular enlargement. Further, the initial study may reveal percentiles no greater than 65, findings which are within normal limits, but re-examinations may demonstrate the percentile values to become elevated to 90, above 100, etc. These changes, while not large in themselves, may be of sufficient magnitude to establish the diagnosis.

In instances of advanced left auricular enlargement the tables are unnecessary and inaccurate. The additional enlargement of an already considerably dilated auricle is mainly to the right in the usual case. Further posterior enlargement occurs only to a comparatively slight extent. Since these measurements are influenced mainly by the posterior expansion, it is clear that any auricular enlargement toward the right would show only little correlation with the percentile values.

DISCUSSION

The apparent accuracy and usefulness of this method in the diagnosis of minimal left auricular enlargement must be further tested by statistical analysis of data compiled from numerous additional observations on normal and abnormal cases. It was thought that some confirmation of the findings might be obtained by comparing the results of the measurements with those following angiocardiography. However, Sussman[28] states that angiocardiography, except possibly in cases of mitral stenosis, cannot routinely outline the periphery of the left auricle with sufficient detail to permit accurate measurements of the exact size of the auricle. Thus, the diagnosis of left auricular dilatation by angiocardiography is qualitative, depending on gross changes in size, shape, position and contour. No exact information of the actual area of the normal and abnormal left auricular shadow can be obtained in all types

of cases with the method in its present state. It would therefore appear that auricular index measurements may give more information concerning minimal enlargement of the left auricle than angiocardiography.

Roentgenoscopic examination of the heart, including study following opacification of the esophagus, is an essential part of every cardiac examination and yields information not obtainable by any other method. It has not been satisfactory, however, for the determination of minimal left auricular enlargement in the borderline case. This inadequacy may be due to several factors: (*a*) roentgenoscopy is a qualitative method; (*b*) the short target-screen distance employed results in considerable magnification and distortion, especially with movement of the patient or screen; (*c*) no permanent record is available for the detailed study apparently necessary in making the diagnosis.

The limited sample of normal controls employed in this study somewhat restricts the use of the measurements for general clinical use. The normal standards were obtained from a population consisting only of healthy, athletic males between eighteen and thirty years of age. Therefore, according to rigorous statistical methods, all comparison measurements in suspected cases are truly valid only for individuals in the same category. It would be highly desirable to establish normal standards for females, the older age group and children. Additional investigation is also indicated for the confirmation of the normal control values presented in this report. These studies may result in slight changes of the normal percentile values without diminishing the basic accuracy and correctness of the method of examination. Experience thus far has indicated that the tables are reasonably accurate for young women, and even for older people who show no gross disturbance in the appearance or course of the aorta and esophagus. The standards are probably inaccurate for infants and young children,[6] however, and should therefore not be employed for this group.

In the presence of conditions which grossly alter the course of the esophagus, the measurements are obviously invalid. A list of the more common conditions affecting the esophageal course includes the following:

I. Esophageal displacement in the region of aortic arch; due to
   1. Aneurysm of aorta.
   2. Aortitis with dilatation.
   Marked tortuosity and dilatation of the aorta, as in hypertension or arteriosclerosis.
   4. Large substernal goiter.
   5. Congenital dextro-aorta.

II. Change in course of the esophagus below the aortic arch; due to
   1. Arteriosclerosis with tortuosity, in which the esophagus is adherent to the descending thoracic arota as the latter takes a tortuous course.[23]
   2. Local mediastinal processes: mediastinitis, tumors, etc.
   3. Mediastinal shifts from extrinsic causes: pulmonary fibrosis, marked pneumothorax, etc.
   4. Dilatation of the esophagus: cardiospasm, carcinoma, etc.
   5. Marked pericardial effusion.

Interference with the measurements by the conditions listed above is only infrequently encountered. The cases suspected of left auricular enlargement usually are in the age group where arteriosclerosis and cardiovascular syphilis are rarely observed. The remaining conditions are uncommon and recognized with comparative ease. Experience with the normal controls has indicated that dorsal kyphoscoliosis, even if severe, does not affect the esophageal course or the validity of the measurements (Fig. 8).

Study of numerous abnormal cases will be required for the determination of the relative individual importance of "theta," "gamma" and "*M.P.*" as accurate indices of left auricular enlargement. Based on the

abnormal cases examined (to be reported at a later date), it is felt that probably the most important index is the "*M.P.*" Values for "gamma" have been observed in the region of the 90th or 95th percentile with normal measurements for "*M.P.*" In these instances "gamma" probably indicates a normal, vertical esophageal direction. When "*M.P.*" is abnormally large, however, "gamma" is usually correspondingly increased. The value of "theta" has not been clearly established. Several cases of undoubted mitral disease have been observed where "theta" was increased beyond the normal range, but in which "*M.P.*" has shown only a high normal value. However, in numerous cases where "*M.P.*" has been found considerably more posterior than normal, "theta" measurements have been within normal limits. It is felt that in the latter instances the coincident upward enlargement of the auricle has caused a flattening of the angle between the posteriorly displaced lower end of the "alpha" segment and the upper portion of the auricular impression (i.e., a diminution in the value of "theta"). At present "theta" is regarded as perhaps the earliest indicator of beginning abnormality, but not the most certain criterion. Whether this opinion is correct or whether "theta" has any real usefulness remains to be determined by further study.

In conclusion, the comprehensive manner in which the subject has been reviewed is believed warranted because a new and somewhat different approach to the diagnosis of minimal left auricular enlargement is presented. Confirmation of the results is highly desirable, and all the details of the method and statistical analysis have therefore been given. Because of the detailed manner of the presentation the method may appear too complex, cumbersome and unwieldly for routine use. In actual practice however, the measurements and interpretation are quickly and easily accomplished.

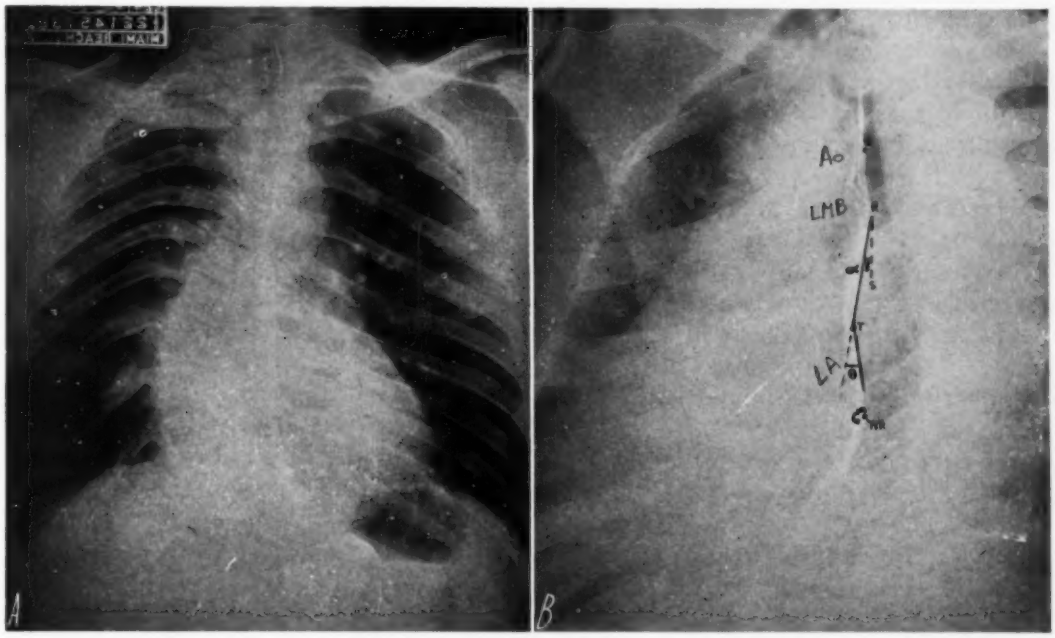

Fig. 8. Appearance of esophagus in a subject with marked dorsal scoliosis. (*A*) Posteroanterior view. (*B*) Right oblique view, mid-inspiration. Note the normal course of the esophagus, which lies adjacent to the heart and does not follow the spine. The esophageal shadow had been intensified for better photographic demonstration. Identifying symbols are the same as in Figure 1.

Only little experience enables the examiner to make the complete study, including the measurements, in from three to five minutes. Indeed, considerably less time is required for this procedure than for the majority of popular pelvimetric analyses. Experience thus far has indicated that the results have adequately compensated for the time and effort expended.

SUMMARY

1. A quantitative method for the determination of minimal left auricular enlargement is described, and the method of measurement presented in detail.

2. Findings in 250 healthy males, from eighteen to thirty years of age, have been used to establish normal control values.

3. The anatomic and pathologico-physiological basis for the method is reviewed.

4. Details of the statistical analysis of the data on the normal control series are given.

5. Tables of Normal Standards are presented.

6. The usefulness and limitations of the method and data are discussed.

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RETROGRADE ABDOMINAL AORTOGRAPHY*†

By P. L. FARIÑAS, M.D.
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IN 1929 dos Santos, of Lisbon, described his method for the arteriographic study of the abdominal aorta and its branches. This method consists essentially in the blind puncture of the abdominal aorta in the paravertebral region at the level of the twelfth dorsal vertebra, followed by the injection of a opaque substance through a trocar 1.2 mm. in diameter at the rate of 4 cc. per second, after which roentgenograms are taken in the posteroanterior position.[1] The patient is given general or spinal anesthesia.

I tried to use dos Santos's blind aortography experimentally in the treatment of cancer of the abdominal organs with certain substances that become fluorescent when exposed to roentgen rays. To avoid the difficulties that arose with dos Santos's method, I began in 1939 to use a new technique for the arteriographic study of the abdominal aorta which was presented at the Forty-first Annual Meeting of the

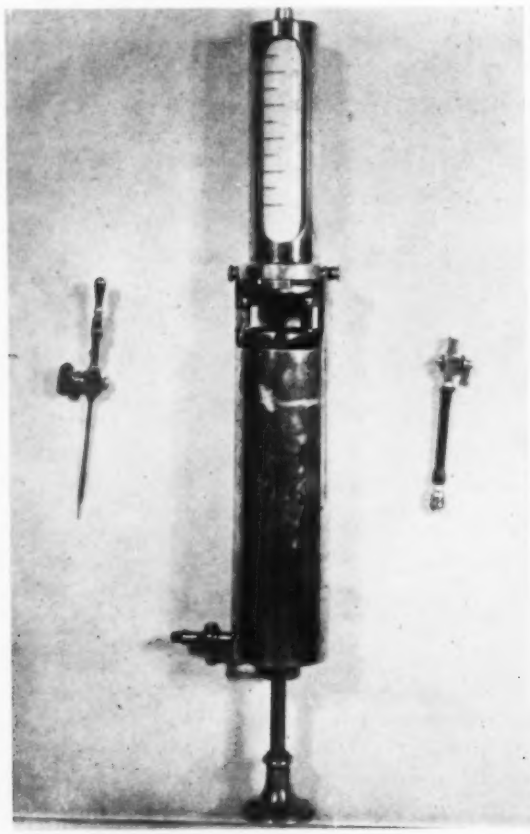

FIG. 1. Necessary instruments: trocar 1.5 mm. in diameter; a 50 cc. syringe; flexible rubber tube that connects trocar to syringe; a pump with a piston that acts upon the embolus of the syringe.

FIG. 2. The patient is placed lying on the plate changer. Everything is ready to begin the injection.

* This work was done at the Cancer Institute in collaboration with Drs. P. Jimenez, Gomez Zaldivar, and J. Casanova, Ph.I.

† Presented at the Joint Meeting of the American Roentgen Ray Society and the Radiological Society of North America, Chicago, Ill., Sept. 24–29, 1944.

American Roentgen Ray Society, at Boston, Massachusetts, in 1940.[2] This technique consists essentially of the puncture of the femoral artery at the level of the triangle of Scarpa with a trocar through which a rubber catheter is introduced and passed into the iliac artery up to the desired level in the aorta, as the case may require. Through this catheter 25 to 30 cc. of a 70 per cent solution of diodrast is injected at the rate of 5 cc. per second. The trocar is then withdrawn, a stitch placed in the adventitia of the artery and the wound closed. Using the same injection urograms are taken after aortography.

In view of the present difficulty, due to war conditions, in obtaining rubber catheters, I was compelled to use instead of "aortography by catheterization" the present "retrograde abdominal aortography." In this method the femoral artery is exposed by blunt dissection, under local anesthesia, at the level of the triangle of Scarpa and punctured with a trocar 1.5 mm. in diameter through which is injected 50 cc. of a 70 per cent solution of diodrast in two and one-half to three seconds. Tourniquets must be placed at the root of both lower extremities in order to produce a slowing of the abdominal circulation. The Trendelenburg position may be required in certain cases. In experiments with dogs, I was able to observe under the roentgenoscope that the opaque substance had to overcome first the inertia and then the blood pressure when it was injected. It reaches a higher level during diastole and descends during systole, entering then into the branches of the abdominal aorta. To avoid changes in pressure when the opaque substance is injected by hand I have designed an apparatus to maintain a constant pressure and rate of injection. It consists of a pump with a piston which acts upon the embolus of the syringe. The piston works by an air compressor with a regulator and a manometer (Fig. 1).

Fig. 4. Aneurysm of the abdominal aorta. The filling defects are due to organized blood clots.

Fig. 3. Advanced atheromatous degeneration of the aorta and iliac arteries. Observe the almost complete stenosis at the aortic cone. The renal irrigation is very poor.

FIG. 5. Very large uterine fibroma. Observe the circulation surrounding the tumor.

FIG. 6. Very large ovarian cyst. Note reduction in the caliber of the arteries compressed by the tumor.

With a trocar 1.5 mm. in diameter and a constant pressure of 15 pounds it is possible to inject 25 cc. of the opaque substance per second, the speed of injection being modified according to the blood pressure and the vascular condition of the patient. The first roentgenogram is taken when 40 cc. of the opaque substance has been injected and the second one immediately afterwards, using a fast plate changer (Fig. 2).

FIG. 7. Retrograde abdominal aortography. Roentgenogram taken when 40 cc. had been injected. The renal circulation is clearly visible.

When the injection is finished, the trocar is withdrawn, a stitch placed in the adventitia of the artery at the site of the puncture and the wound closed. I have had no accidents with this method. The patient should be given a barbiturate the night before and morphine hypodermically one hour before the injection in order to obtain relaxation and avoid pain.

With retrograde abdominal aortography pathologic changes of the aorta and its branches can be clearly visualized and

studied (Fig. 3 and 4). It represents an important contribution to the diagnosis of abdominal tumors (Fig. 5 and 6), and through the visualization of the arterial circulation of the kidneys (Fig. 7) valuable information is obtained concerning the renal secretory and excretory functions, for which the urograms taken at the same moment are an important adjunct. The method thus affords a means for further study and understanding of renal pathology.

The physiology and pathology of every organ are so intimately related to its circulation that the importance of its study cannot be overemphasized. It is hoped that retrograde abdominal aortography will become a common method of diagnosis and clinical investigation, now that its technique is reduced to that of simple arteriography.

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RIGHT-SIDED AORTIC ARCH*

CASE REPORT

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As roentgen examinations of the chest become more routine, the number of right-sided aortic arches diagnosed during life has become more numerous. However, up to this time, the total number of cases reported in the literature apparently does not exceed 30. Since it is still a fairly uncommon occurrence, the following case is being reported. It was found purely as an incidental finding in a soldier who came to the hospital because of pain in the abdomen.

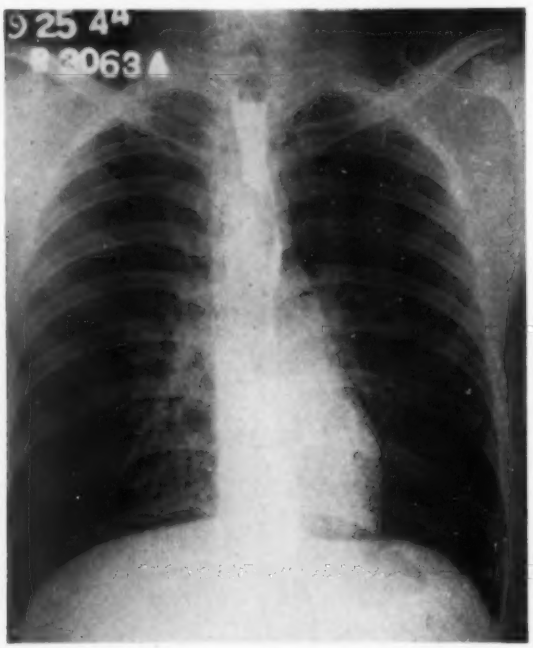

Fig. 1. Posteroanterior roentgenogram of the chest. The characteristic displacement of the esophagus to the left of the aortic arch is demonstrated. There is no right-sided aortic knob which may have led to an earlier diagnosis of the anomaly on a previous roentgenogram, had it existed.

The importance of recognizing the presence of a right-sided aortic arch is mainly due to the fact that at times it may explain the presence of dysphagia and pressure symptoms under the sternum. In the presence of these symptoms and a right-sided aortic "knob," the mistaken diagnosis of a mediastinal new growth has been made and the patient submitted to thoracotomy. Such a case has been reported by Garland in his comprehensive article on this condition.

For full details of the anatomy, types, differential diagnosis, embryology, and roentgenological characteristics of right-sided aorta, readers are referred to the reports by Garland and by Eisen.

Fig. 2. Right anterior oblique view of the chest. The anterior displacement of the esophagus by the right-sided aortic arch is shown.

* From AAF Regional Hospital, Hammer Field, Fresno, California.

CASE REPORT

Male soldier, married, aged twenty-three, and having had two years of service in the Army, came to the Department of Roentgenology from a near-by military installation for gastrointestinal examination on September 20, 1944, because of pain in the abdomen of four to six months' duration. The pain grew worse about one hour after meals and sometimes woke the patient at night. The patient also vomited about three to four times a week. The pain was partly relieved by soda. Food and milk gave complete temporary relief. The patient had not vomited blood, had no tarry stools, diarrhea nor constipation. Physical examination was negative.

On roentgen examination, the thin barium sulfate suspension was retarded in its descent at the level of the aortic arch which was found to lie to the right (Fig. 1) and posterior (Fig. 2) to the esophagus at this level. This displacement of the esophagus to the left and anterior to the aortic arch is the outstanding roentgen appearance due to the anomaly. There was no right-sided aortic "knob." This is no doubt the reason the anomaly was not suspected in a posteroanterior roentgenogram of the chest taken the year before. The rugae of the stomach were rather coarse. The duodenal cap had a persistent cloverleaf outline and a niche in the center.

The patient was then admitted to the hospital on October 3, 1944, for treatment. Laboratory studies of the feces and blood were normal on three occasions. The Kahn test was negative. The gastric analysis showed 83 per cent of free acid. The electrocardiographic study was within normal limits.

The patient was placed on a Sippy regimen, amphojel, tincture of belladonna, then a soft bland diet followed by a soft diet, and finally a regular diet. He became asymptomatic and gained weight and was discharged from the hospital to full duty on November 14, 1944.

SUMMARY

A patient with a right-sided aortic arch is reported. He had the characteristic displacement of the esophagus to the left and anteriorly to the arch. It was a purely incidental finding and caused no symptoms.

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The author wishes to express his gratitude to Captain Raymond E. Cronemiller, M.C., for the clinical data he obtained to make possible this report.

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THE SUPINE PROJECTION IN THE DIAGNOSIS OF LESIONS OF THE CORPUS AND POSTERIOR WALL OF THE STOMACH

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I. METHOD

ROENTGENOGRAMS of the stomach in the supine position, used mainly for the study of the cardia and fundus, have been superseded by upright views in recent years and are now resorted to only exceptionally. A survey made during the past eighteen months suggests, however, that the supine projection is useful for the detection of lesions of the posterior wall and corpus of the stomach, for the following reasons:

In the prone position, the fundus points upward and the gastric mid-third is lowest; accordingly, gas rises into the fundus and the contrast medium tends to accumulate in the corpus. Since at the same time the contents of the antrum are displaced towards the midline by the pressure of the spine, the opaque medium, forced into the corpus from both sides, often casts a dense shadow which may obscure small or shallow abnormalities in this region—particularly in obese and stocky subjects, in whom the increased anterior convexity of the stomach favors the mechanisms just described. In the supine position, conditions are reversed. The opaque medium flows into the fundus, and gas ascends into the corpus. When the entire stomach is filled first, by placing the patient upright or prone, small amounts of contrast medium are retained in the rugae of the corpus and antrum but most of it flows back into the fundus as soon as the supine position is assumed. The resulting thin coating of the corpus and antrum, together with the gas rising into the corpus, produce in this region a double-contrast mucosal pattern in which lesions often stand out clearly. Owing to gravity,

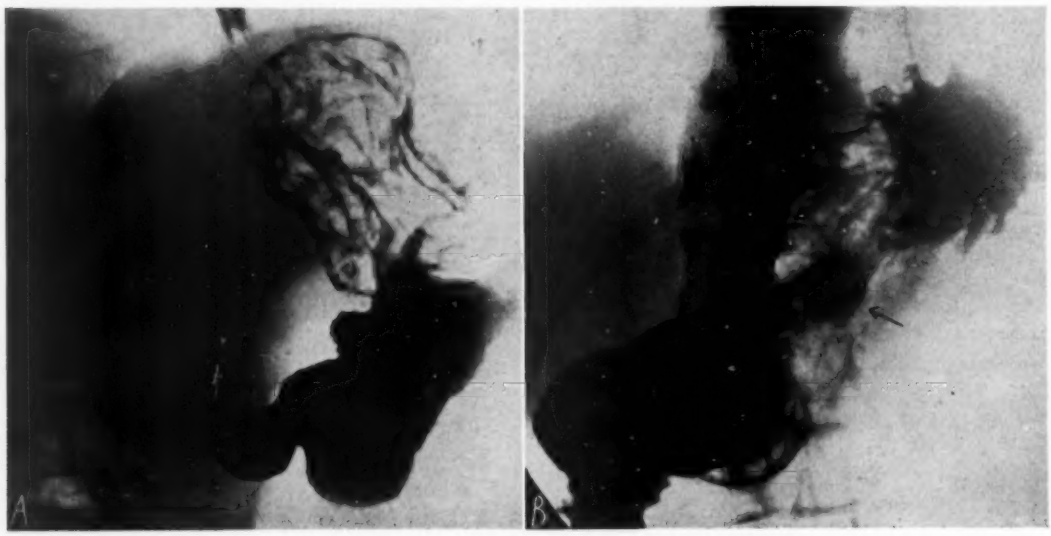


FIG. 1. The patient is a male, aged fifty-two, with gastric distress. The large ulcer of the posterior gastric wall was not seen in the prone oblique (*A*) and prone positions, but is well shown in the supine position (*B*).

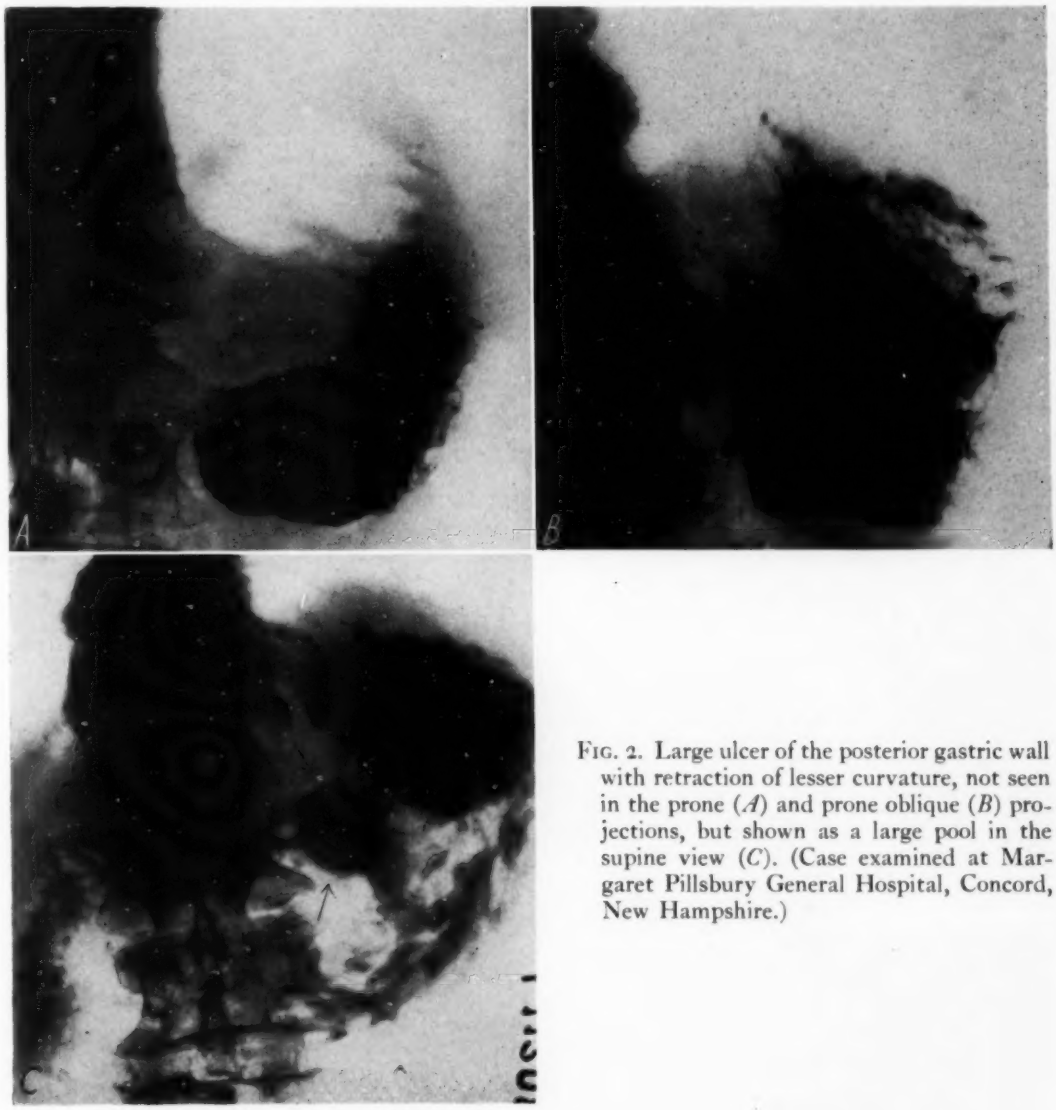


Fig. 2. Large ulcer of the posterior gastric wall with retraction of lesser curvature, not seen in the prone (*A*) and prone oblique (*B*) projections, but shown as a large pool in the supine view (*C*). (Case examined at Margaret Pillsbury General Hospital, Concord, New Hampshire.)

ulcers and craters of the posterior wall are usually empty, and invisible, in the prone position, but are apt to be filled, and visible in the supine position (Fig. 1 and 2). Small intragastric prominences, such as caused by incipient tumor, displace more readily the thin layer of opaque medium which is present in the corpus in the supine position than the more massive filling of this region usually present in the prone position, and are therefore seen as filling defects more easily in the supine projection (Fig. 1 and 6). All these factors often combine and cause two cardinal signs of gastric pathology—crater and filling defect—to appear more distinctly in the supine than in the prone projection, provided the lesion has its seat in the posterior wall and/or corpus of the stomach.

II. ROENTGENOGRAPHIC TECHNIQUE

In order to distribute the opaque medium through the stomach, the patient is placed upright and prone for a few minutes previous to making supine views. The changes of position incident to roentgenoscopy are sufficient for this purpose. When this preliminary procedure is

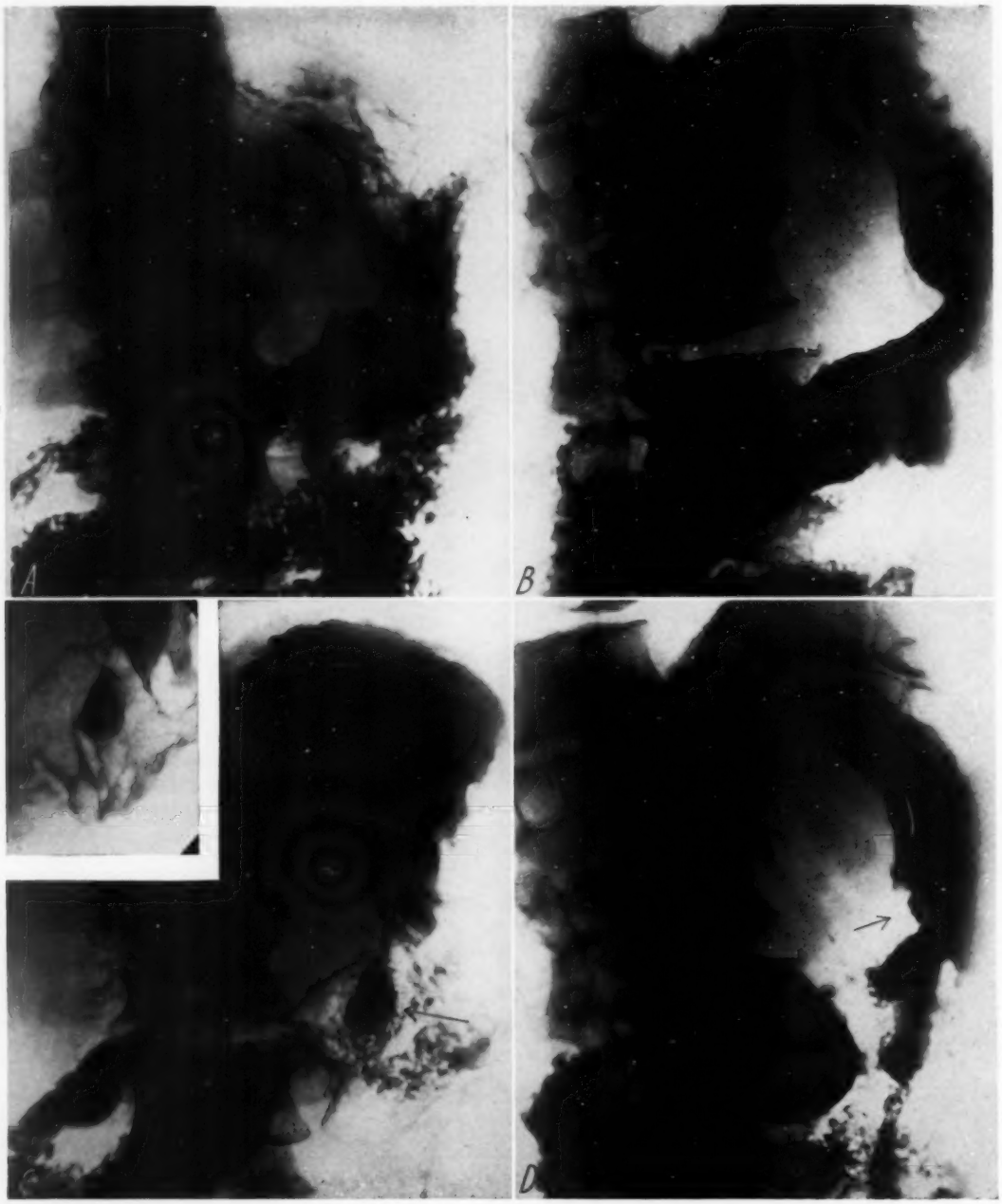


Fig. 3. Large ulcer of posterior gastric wall, not recognized in the prone (*A*) and prone oblique (*B*) projections, but demonstrated by straight supine (*C*) and oblique supine (*D*) views. Despite the meniscus effect seen in *D*, the ulcer proved to be benign. Insert: spot roentgenogram of crater.

omitted, the opaque medium is usually retained in the fundus, with no or insufficient filling of the corpus and antrum. On the other hand, once the need for supine views has been established by roentgenoscopy, too much time should not elapse before placing the patient supine, lest the duodenum and jejunum fill massively and overshadow the gastric mid-third, thereby causing a criss-cross pattern

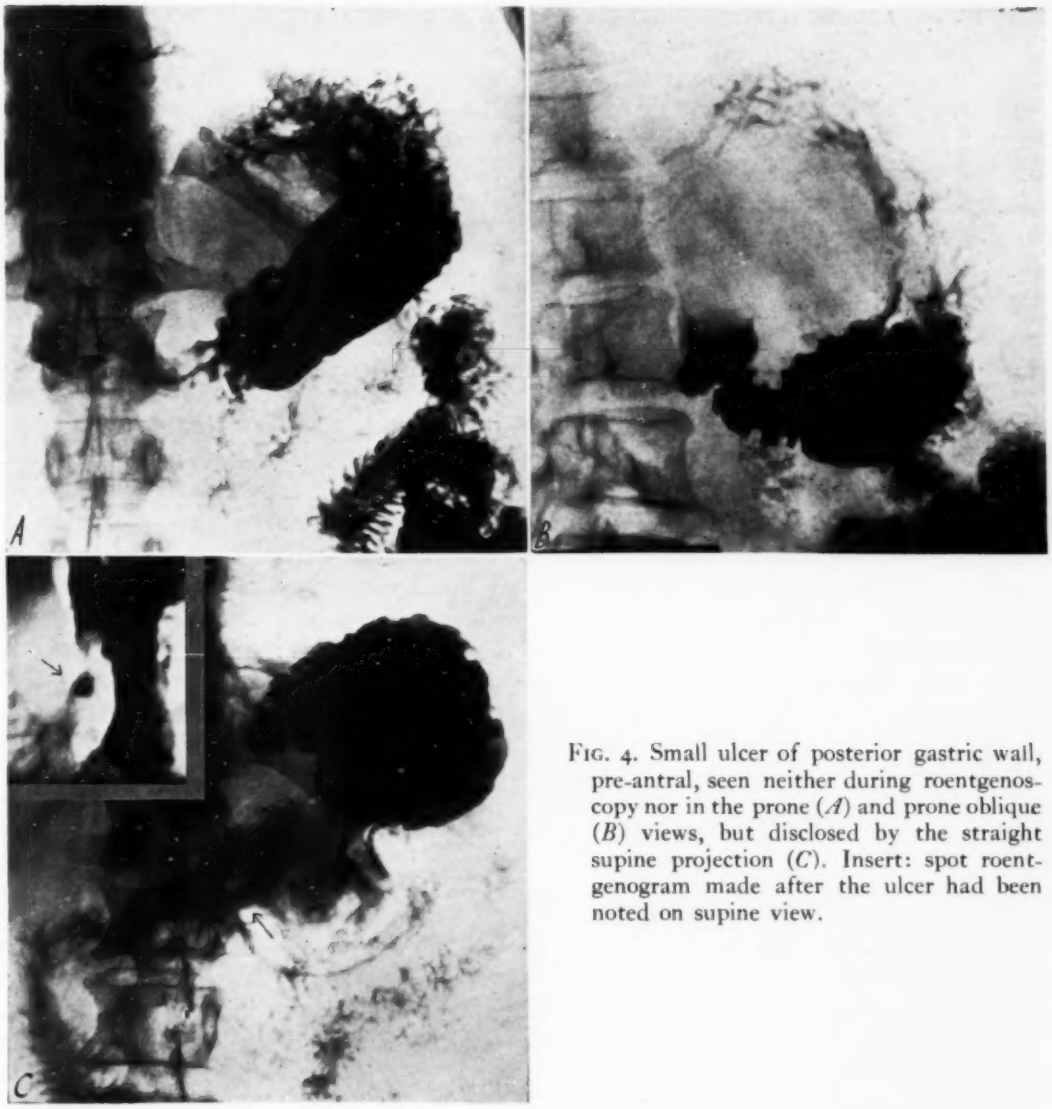


Fig. 4. Small ulcer of posterior gastric wall, pre-antral, seen neither during roentgenoscopy nor in the prone (*A*) and prone oblique (*B*) views, but disclosed by the straight supine projection (*C*). Insert: spot roentgenogram made after the ulcer had been noted on supine view.

in which significant details become easily lost. This superimposition of shadows is particularly troublesome when the opaque medium runs rapidly through the stomach and floods the small intestine. It is then best to wait until stomach and proximal small bowel are empty and to repeat roentgenography in the supine projection immediately after administration of a second opaque meal.

Two positions have been found useful: one, straight supine, with the patient flat on his back; the second, oblique supine, with the patient on his back and the right side raised by about 45 degrees. Since the corpus and antrum ascend in the supine position and the pylorus is more to the right because there is no compression by the spine, the tube has to be centered about 2 inches higher and 1 inch more to the right than for the prone projection.

The exposure factors are the same as for the prone projection in slender patients, but higher penetrations than for the prone projection are needed in obese and stocky persons, since the heavy abdominal tis-

sues, not being compressed by the weight of the body as in the prone position, add to the thickness of the part examined.

The straight supine projection is helpful mainly for the demonstration of lesions of the gastric mid-third; the oblique supine, for lesions of the posterior wall close to the fundus.

III. FINDINGS

The appearances presented in the supine projection differ appreciably from the familar gastric image known through the prone projection. Some practice and experience are needed to interpret supine views. The fundus, pylorus, and duodenum are rarely shown satisfactorily in the supine projection. Supine views are not intended to, and cannot, supplant the other well established projections; but lesions of the corpus and antrum, particularly in the posterior wall, have often been discovered in the supine projection after having escaped detection by other procedures, including roentgenoscopy and spot roentgenograms (Fig. 4, 5, 6, 7, and 8). Although it is sometimes held that practically all lesions can, or should, be disclosed by adequate roentgenoscopic examinations, the need for proper roentgenographic records is evident. The supine and supine oblique projections, though merely additional records, often yield the essential information.

Among lesions well shown by supine views, large ulcers of the posterior gastric wall have been conspicuous (Fig. 2 and 3). The fact that large rather than small ulcers may be easily overlooked has long been known, although it is not emphasized in current texts. The observations indicate that opaque medium is more apt to be retained in the narrow tip of a small ulcer than in the shallow pit of a large ulcer. When located in the posterior wall, a large ulcer usually empties like an overturned saucer or cup in the prone position and is then invisible, but fills and appears as an opaque pool in the supine position (Fig. 2 and 3).

As already mentioned, there is only a thin layer of contrast medium in the corpus in the supine position, since the anterior

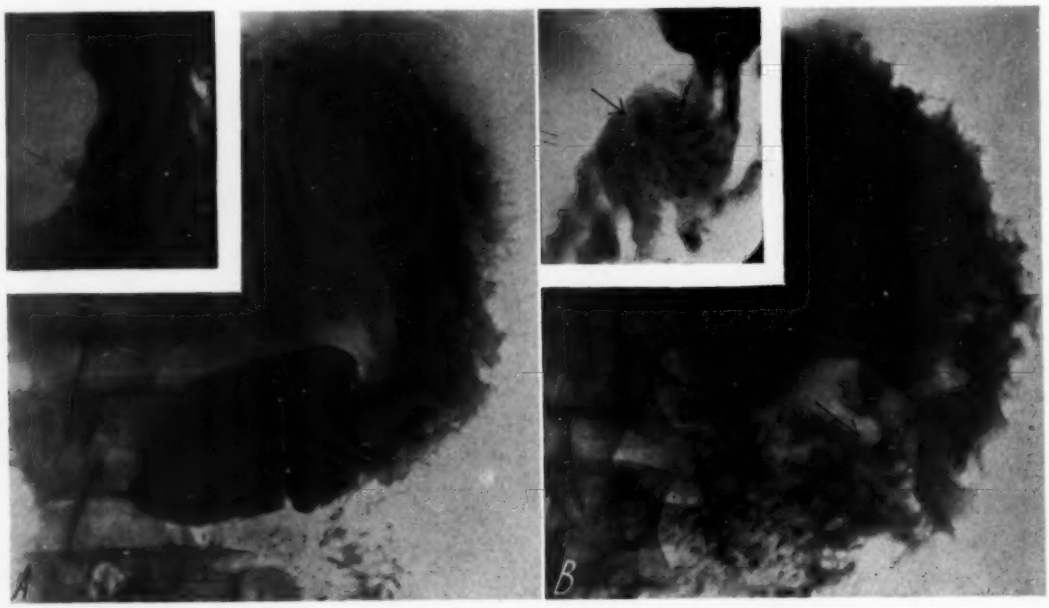


Fig. 5. Small ulcer of posterior gastric wall close to the cardia, not visible during roentgenoscopy and in the prone (*A*) and prone oblique views, but revealed by supine projection (*B*). Inserts: spot roentgenograms made after discovery of the ulcer by supine view.

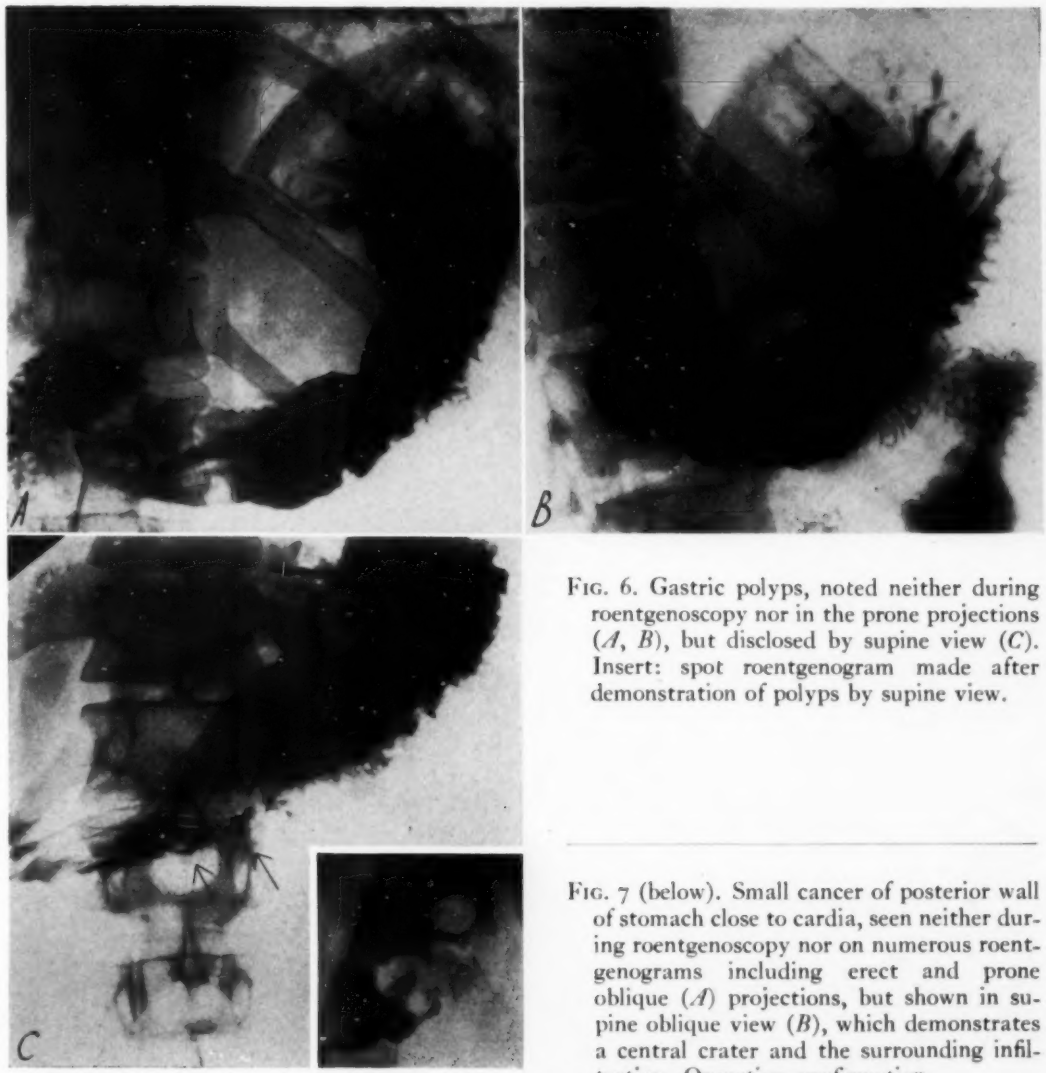
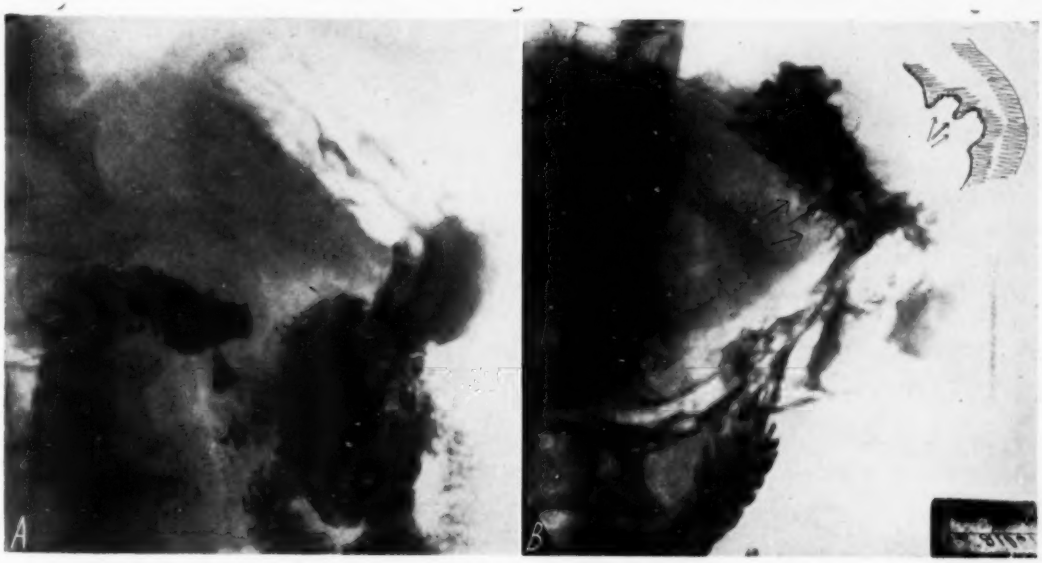


Fig. 6. Gastric polyps, noted neither during roentgenoscopy nor in the prone projections (*A*, *B*), but disclosed by supine view (*C*). Insert: spot roentgenogram made after demonstration of polyps by supine view.

Fig. 7 (below). Small cancer of posterior wall of stomach close to cardia, seen neither during roentgenoscopy nor on numerous roentgenograms including erect and prone oblique (*A*) projections, but shown in supine oblique view (*B*), which demonstrates a central crater and the surrounding infiltration. Operative confirmation.



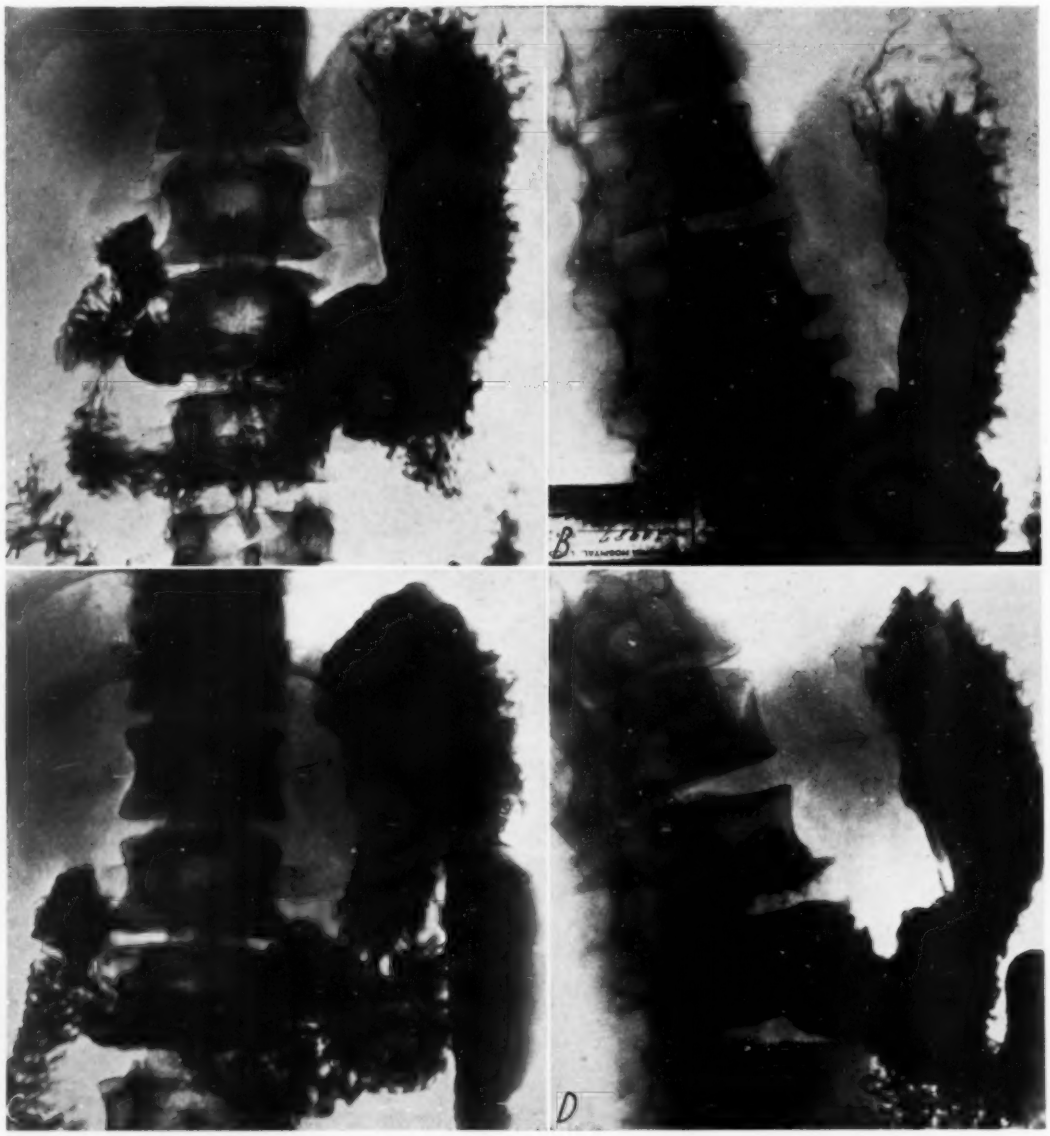


Fig. 8. Small ulcer of posterior gastric wall close to cardia, overlooked during roentgenoscopy and in the prone projections (*A*, *B*), but shown by straight supine (*C*) and supine oblique (*D*) views. There had been a profuse hematemesis one week previous to examination.

and posterior gastric walls are virtually in contact in this projection. Small tumors cause filling defects more distinctly in this thin layer than in the more massive filling present in the prone and prone oblique views (Fig. 6). The differentiation of intragastric tumors from pressure defects caused, e.g., by neoplasm of the pancreas and retrogastric nodes, has to be made by the usual methods.

Large tumors of the cardia are often seen in the upright position, but small cancers of the posterior wall of the fundus and cardiac region may be visible in the supine oblique view alone (Fig. 7). Since this region is frequently inaccessible to palpation during roentgenoscopy because of the overlying ribs and ensiform process, these lesions are easily overlooked. Similarly, benign ulcers at this site, which are said to

Fig. 9. In the supine and supine oblique projections, the opaque medium usually flows back into the fundus and esophagus, thereby outlining small lesions of these parts. Peptic ulcer of lower end of esophagus (confirmed by esophagoscopy), not seen in the prone oblique view (*A*), but disclosed by supine oblique view (*B*). Small hiatus hernia, not shown in prone projection (*C*), but revealed by supine view (*D*).

occur mainly at advanced age, are usually revealed by the supine oblique projection more clearly than by other views (Fig. 8).

The ridges and furrows of the gastric mucosa appear broader in the supine than in the prone position; this should not be interpreted as an indication of gastritis.

The fact that hiatus hernias may be

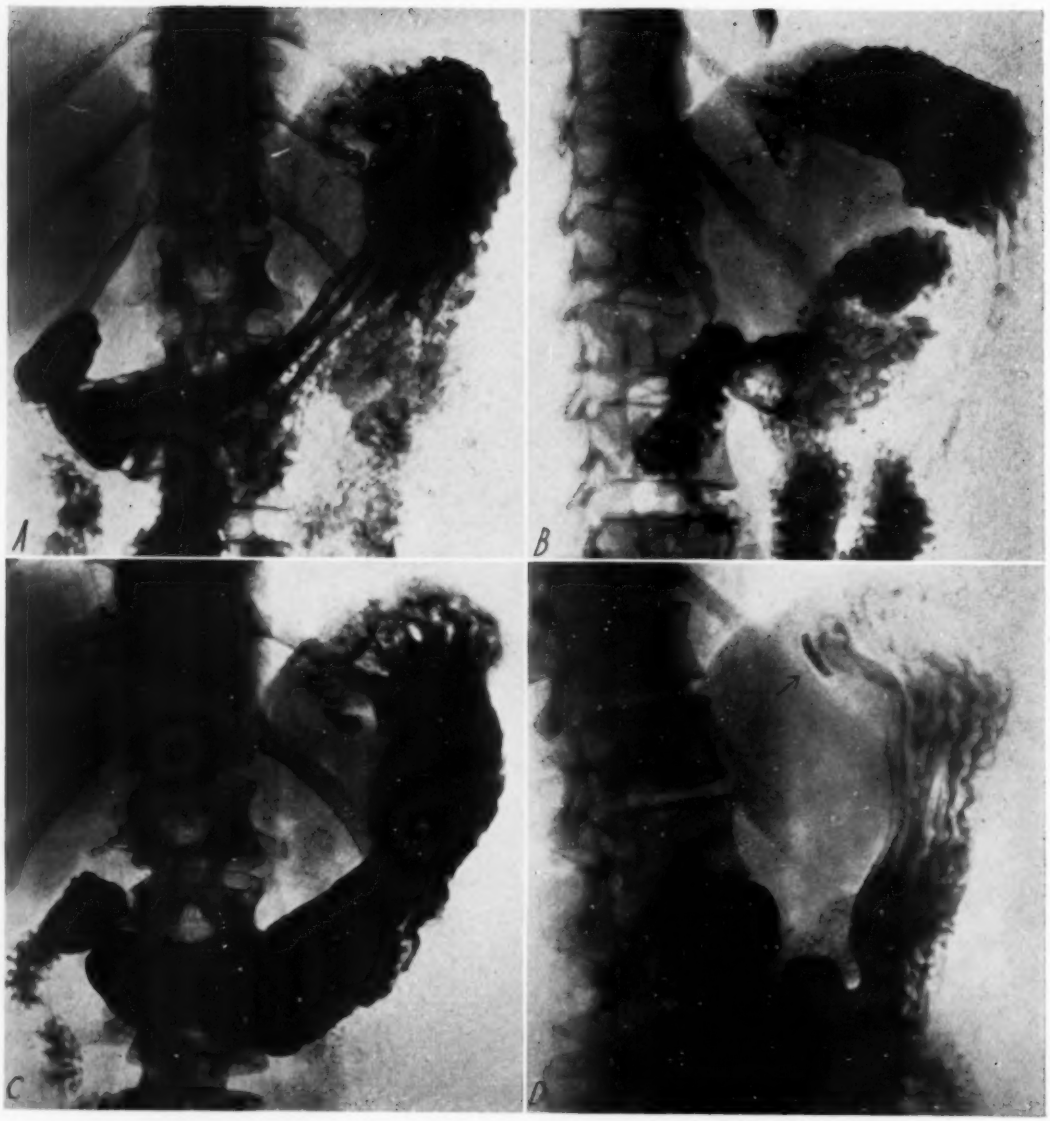


Fig. 10. Small diverticulum of stomach, shown more clearly by supine (*A*, *B*) than by prone (*C*, *D*) projections, as a result of better filling of fundus and cardia in the supine position.

visible only in the supine position was confirmed by the results of this survey. It was further observed that in the supine and supine oblique projections the opaque medium usually flows back into the esophagus in these cases, thereby outlining not only the whole extent of the herniation, but also additional abnormalities, such as peptic ulcers of the esophagus (Fig. 9).

IV. CONCLUSIONS

The results here reported may suggest that findings obtained with the supine projections may also be disclosed by spot roentgenograms, at least in most instances. In many patients, however, the lesion was not suspected during roentgenoscopy and was not recognized until supine views revealed it; consequently spot roentgeno-

grams of the involved areas were omitted and a negative report would have been given if supine views had not been made. Most of the spot roentgenograms shown in this paper were made not during the first roentgenoscopy, but after discovery of the lesion by supine projections.

Notwithstanding its incontested value, the spot roentgenogram method is not innocuous. The amounts of radiation absorbed by the examiner are significant enough to cause damage. Severe burns of the neck and upper chest, sharply delineated by the upper edges of the protective aprons, were observed in two radiologists in their early thirties. It is questionable whether such risks should be taken for the sake of a purely diagnostic procedure. Further, the long periods spent during detailed spot roentgenogram studies of series of patients sometimes cause visual fatigue responsible for poor diagnostic results. The method should be applied judiciously rather than routinely. In more cases than seems to be realized, an accurate roentgenographic technique yields results that are equal to those obtained with spot roentgenograms.

The supine and supine oblique projections are examples to illustrate this point. For the purpose of this survey they were used routinely in all cases for several months; but this was found to be unnecessary. In conjunction with roentgenoscopy, prone, prone oblique, and upright views reveal the morbid condition present in the stomach in nearly 80 per cent of the cases. In the remaining 20 per cent, supine projections are of value and may demonstrate lesions not disclosed by other methods, especially when the corpus and posterior wall of the stomach are involved. In other words, the number of positive findings can be definitely increased by this technique.

The observations suggest that roentgenography of the stomach in the supine and supine oblique projections is indicated when the clinical manifestations strongly point to a gastric lesion but the usual roentgen methods fail to reveal such a lesion.

V. SUMMARY

1. Owing to anatomical and physical factors, roentgenograms of the stomach in the supine and supine oblique projections often disclose lesions of the corpus and posterior wall which are either invisible or not clearly shown in other views.

2. The supine and supine oblique projections cannot supersede the other established projections but may yield additional, and often essential, information in this group of cases.

3. The supine and supine oblique projections are indicated especially when a gastric lesion is suspected on the basis of the clinical manifestations but fails to be shown by the usual roentgen methods.

Laconia Hospital
Laconia, New Hampshire

THE COAGULOGRAM AS A CRITICAL INDICATOR OF IRRADIATION EFFECT

PRELIMINARY REPORT* BASED UPON A SEVEN YEAR SURVEY OF THE PERSONNEL OF THE DEPARTMENT OF RADIOLOGY, ROYAL VICTORIA HOSPITAL

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(*With the Collaboration of* CARLETON B. PEIRCE, M.D., *Radiologist-in-Chief, Royal Victoria Hospital*)

OUR problem and observations concerned themselves with the safety of personnel employed in the Department of Radiology of the Royal Victoria Hospital over a period of seven years with particular emphasis on the effects of minimal irradiation upon the coagulogram and the hemogram as a whole. The employee is likely to be exposed to small intermittent doses of radiation spread over a long period of time.

The effects of minimal exposures of the body tissues to radiation have hitherto been gauged by a blood survey, more particularly limited to the cytological elements of the blood, with special interest in the comparison of the red blood cell, hemoglobin, white blood cell, and platelet status with the normal findings. In many instances there was no knowledge of the previous hematologic status of the employed personnel, their general health, habits, diet and other features which may affect the hemopoietic system.

The findings in those studies, although indicative of damage to the hemopoietic system, particularly in excessive irradiation in many instances, do not seem to satisfy the requirements of radiologists in general. They are, as a rule, more anxious to have at their disposal a method by means of which warning signs of early adverse irradiation effects would indicate that precautions should be taken to prevent or eliminate further damage to the individual who shows this excessive sensitivity or may not have followed the prescribed technique in his daily work.

We felt that a study of the possible effects of irradiation on other members of the complex hemopoietic system, with particular reference to the coagulation mechanism, might give added information of value.

The present report concerns itself with complete blood studies of both professional and technical personnel apt to be exposed to minimal irradiation in the course of their routine work, with particular emphasis on the study of the coagulogram. In the latter study, more intensive observation was devoted to the mechanism of coagulation of the blood; namely, fibrin time, coagulation time, prothrombin concentration, and blood platelets.

The liver plays a proper rôle all through life, in some of its functions, at least, as a member of the hemopoietic system. We accept the view that the liver has as one of its main functions the production and elaboration of prothrombin, one of the delicate rôles in the complex hemopoietic system which is attributed to this organ. It is quite possible that this specialized function of the liver may react with greater sensitivity to minor overstimulation or to actual injury by a manifestation of an altered blood prothrombin concentration. No further justification is needed for including the coagulation mechanism studies in our hemogram surveys.

* Prepared for the Section on Surgical Radiology, Sub-Committee on Surgery, Associate Committee on Medical Research, National Research Council, of Canada. Published with the permission of the Associate Committee on Medical Research, whose financial assistance in the investigation is acknowledged with appreciation.

REVIEW OF THE LITERATURE

The stated effects of minimal irradiation on the hemopoietic system of roentgen-ray and radium technical personnel varies with the reports of the various observers, with the type of observation made, the susceptibility of the individuals employed, the hemopoietic status before employment, the frequency of repeated examinations, the time and examination and the amount of exposure involved. A great deal is not fully understood nor explicable. Many observers[3,4,5,6,7] including our own group suspect that small doses of radiation are irritative in their effects, in that reproduction and maturation seem to be intensified, and consequently cells seem to age more rapidly.

It is generally accepted that the effects of irradiation depend on the dosage, frequency of irradiation, route of entry, idiosyncrasy of the individual and the size of the area exposed.

Excessive exposure to radioactive substances may result in severe and even fatal aplastic anemia.

In the case of external irradiation received inadvertently by radium and roentgen-ray workers, or deliberately as a therapeutic measure, it is generally stated that the leukocytes are primarily affected, resulting in a leukopenia due to reduction of neutrophiles. Lymphocytosis, lymphopenia or monocytosis may develop. Eosinophilia has been observed as a result of overexposure. Platelets are very resistant to roentgen rays and may even increase under this influence. At any rate severe reduction of platelets is unusual. This is important in the light of the present communication. Red cells are more often increased than reduced under the moderate or minimal exposure, as is also the total hemoglobin. Large and excessive doses are opposite in their effects, producing anemia, leukopenia and thrombocytopenia.

The effects of internal irradiation with the radioactive isotopes are as yet incompletely known. Here, however, as well as in alpha radiation of dial painters, there have been observed, regardless of the mode of administration, an initial erythrocytosis, and the other initial irritative responses noted above. The eventual results are a fibrosed marrow and even sarcomatous changes.

Pioneer workers with roentgen rays were quite aware of the possible deleterious effect of exposure on the hemopoietic system. Roentgen rays and radium were known to affect the erythropoietic tissue, and even leukemia among these workers has been reported in the literature. The incidence of such disease in this occupation, however, is not greater than in other occupations, according to Neilsen[14] and hence needs more careful corroboration. Davey and Whitby have seen only one case of leukemia in a fifteen year study of the blood of roentgen-ray workers and radium workers, with a large series of control studies. On the other hand, Levent[9] stated that leukemia was five times as common in physicians practicing radiology, as in their colleagues. It is difficult to exclude coincidence.

Rats and mice seem to show an increase in lymphocytes when subjected to small doses of soft rays; the opposite was obtained by large doses (Murphy[12]; Russ, Chambers, Scott and Mottram[19]). Aubertin and Beaugard[1,2] obtained the opposite result with external irradiation in experimental animals.

Martland,[11] and Rosenthal and Grace[17] showed that with internal irradiation (radium in trade radium workers, and feeding rabbits with radium sulfate) there is definite marrow stimulation, and leukemic changes may be manifested. Roentgen-ray workers are usually subjected to irradiation ranging from moderately soft scattered roentgen rays to those approaching the order of gamma rays. A trade employee is more commonly irradiated from within by alpha rays. External irradiation may eventually result in aplasia. Internal irradiation produces disordered hemopoiesis. Rolleston[16] reported 12 cases of aplastic anemia due to external irradiation; 7 were

in radium workers, 4 due to roentgen rays, and 1 in a thorium worker.

Martland[11] definitely showed that internal irradiation with alpha rays affects the marrow, resulting in pancellular reduction and output, consequent anemia and hemorrhagic tendency. The marrow becomes acellular and even fibrotic. This condition is met with in industries where workers openly use and may ingest radioactive substances.

Roentgen rays may depress marrow function. Roentgen-ray personnel are always concerned lest they develop bone marrow damage in the performance of their routine duties, even with the present modern means of protection. Exposure to large doses may do damage to the hemopoietic system. Generally speaking, it is very unusual to find permanent damage in personnel administering ordinary therapeutic exposures. The experimental work on dogs by Shouse, Warren and Whipple[20] speaks for itself.

Martland[10] reviewed the entire subject in 1929 and noted altered hemopoietic tissue after exposure to roentgen rays and alpha rays of radium or mesothorium. He cites Rud, who found leukopenia in 17 nurses, physicians and technicians handling radioactive substances, and Jaulin, who reviewed 17 deaths considered the result of contact with irradiation. Martland insisted that despite all precautions there is danger to roentgen-ray personnel of a possible aplastic anemia or even leukemia. Naegli[13] cited several cases of aplastic anemia from irradiation.

Tripoli and Haam[21] claimed that thorium dioxide does not affect the bone marrow. Pohle and Ritchie[15] have noted aplastic anemia resulting from injection of small doses of this substance into rabbits. Kracke stated that even excessive sunlight may depress the bone marrow activity.

Kornblum, Boerner and Henderson[8] claimed that therapeutic irradiation affects the blood very little, does not affect circulating cells but may cause mild depression of the hemopoietic system. They considered that lymphocytes, neutrophiles, monocytes, eosinophiles and basophiles are affected in the order named.

PRESENT SURVEY

Our observations consisted of repeated studies on the employed personnel of the Department of Radiology of a large general hospital. At the same time of the day, a complete hemogram, consisting of erythrogram, leukogram, and coagulogram, was done periodically on every member of the staff. Particular attention was paid to the coagulogram components to determine how critical they were as indicators of irradiation effects. The other findings were also compared.

The report is based on a seven year survey of the blood examinations of the personnel including all members of the department, male and female, regardless of their technical duties. These included secretaries, stenographers, lay technicians, nurse technicians, and physicians, in both diagnostic and therapeutic divisions.

The main problem was to follow the blood status of the various members of the staff from the hematological angle from employment through any changes appearing during the continuance of their employment, regardless of the nature of their duties. Particular emphasis was placed on the blood of those directly engaged in the various branches of the laboratories where there was a varying opportunity for measured or unmeasured exposure to radiation. This communication concerns itself with the general survey of only the technical and professional staff of 33 individuals. The clerical personnel, not exposed to radiation, showed a different pattern similar to that of other normal non-exposed controls. Some had as many as five examinations per year, others only one examination; the latter were movable personnel, temporarily on duty and transferred to other hospitals before re-surveys were made.

Technique of Investigations.

In an effort to eliminate personal technical errors, only specially trained members of the hematology staff were employed. They are quite familiar with every procedure, and great effort is made at all times to utilize standard instrumental observations with repeat detailed checks in order to minimize personal technical errors.

Proper, repeated standardization of glassware, centrifuges, photoelectric colorimeters, sedimentation tubes, hemoglobin tubes, pipettes, hemocytometers, syringes and the thromboplastic substance employed is vitally necessary. No emphasis is too great on the standardization of glassware.

ROYAL VICTORIA HOSPITAL

DEPARTMENT OF MEDICINE

DIVISION OF HAEMATOLOGY

Date

Case No.
Name Sex Age Ward Dept No.

Provisional Diagnosis Final Diagnosis

1. RBC. 2. Hbg. % (g/100cc) 3. C.I. 4. WBC.
(vol. % oxygen carrying capacity).

RBC MORPHOLOGY

5. Fresh Smear
6. Stain employed 7. Staining qualities
8. Polychromatophilia 9. Reticulocytes 10. Stippling
11. Megaloblasts Erythroblasts Normoblasts Microblasts
12. Macrocytes Microcytes Poikilocytes 13. Micrometry
14. Abnormal nuclear characteristics
15. Sedimentation-rate: 1st hour
2nd hour
16. Fragility 17. Compact cells
18. Mean Corp. Vol 19 Mean Corp Hbg. 20. Mean Corp. Hgb. Concentration
21. Parasites

WBC.

22. Mbl. Pr.Ml. Myel. Met.Ml. Stab. Poly. H.Poly. Eosin. Mast. Lymphbl. Lymph. L. S. Mono.

23. Granules in neutrophilic cells:
24. Oxydase reaction 26. Shift to Slight Moderate Marked
25. Nuclear index
27. Supravital Stain

THROMBOCYTES:

28. No. 29. Morphology
30. Bleeding time 31. Coagulation time: Starting Complete with Calcium
32. Clot retraction
33. Colour of Serum 34. Prothrombin Time 35. Takata Ara.
36. Rumple Leeds

RESUME AND CONCLUSIONS:

FIG. 1

The possibility of slight variation in the individual subject from day to day must be recognized and certain allowances provided for or obviated, especially when one considers the possible hourly variations under varying physiological conditions. For example, a white blood cell count may vary

considerably between morning and afternoon estimation, under the influence of severe exercise, mental strain, proximity to meals, type of meals, etc. The human factor both as to condition of patient and technician has also been taken account of.

We draw attention to the fact that the physical and mental condition of those examined is carefully ascertained as is also their dietetic and clinical history, their working and living conditions. In short, a careful survey of everything that might influence the findings is noted.

Fig. 1*a*. Reverse of chart shown in Figures 1 and 2.

Every examination consisted of some thirty-six manipulations as per the appended chart (Fig. 1). Venous and capillary blood samples were taken, usually in the morning after an ordinary breakfast. The coagulogram was done on fresh unoxalated venous blood. Capillary blood was used for primary and secondary studies and corroboration of findings. Oxalated blood using 0.5 cc. of 2 per cent potassium oxalate to 5 cc. of blood was used mainly as a reserve for control counts, but also for sedimentation rates. The sedimentation rate reading was corrected by 1.09 to allow for cell shrinkage.

Red cell estimations are recorded in terms of the hematocrit readings and hemocytometer counts, using 3.5 per cent sodium citrate as a diluting fluid in the latter procedure.

Hemoglobin determinations were done with a photoelectric colorimeter, whose calibration was checked daily, and results are given in both percentages and grams.

> 100 per cent hemoglobin is equivalent to 15.6 grams hemoglobin per 100 cc. blood, which in turn is equal to 20.0 volume per cent oxygen-carrying capacity.

Mean hemoglobin concentration readings were arrived at in the usual arithmetical manipulation.

$$\frac{\text{grams hemoglobin} \times 100}{\text{compact cells}}$$

White blood cell counts and differential examinations were made in the usual way. Staining was done by the Pappenheim method.

Fresh smears, cresyl blue smears, neutral red and *janus green supravital smears* were examined in all cases.

The coagulogram (see Fig. 2), which is an important part of our hemogram, received particular attention. Careful study is made of the platelets, their number and morphology in both fresh blood and stained slide, as well as counts in the usual way; clot retraction, bleeding time, fibrin time, complete coagulation time and prothrombin time (done with beef-lung thromboplastic substance).*

The methods employed in the details of all these procedures are standard practice. We adjust our thromboplastic substance to give the range of normal prothrombin time between twenty-five and thirty seconds. We find that a moderately potent thromboplastin lends itself to easier and more accurate readings than one which permits only a few seconds.

TABLE I

ERYTHROGRAM

		EXPOSED PERSONNEL		
		Average	Maximum	Minimum
Red blood cells (Normal)				
Male	(5,000,000)	5,470,000	6,440,000	4,900,000
Female	(4,500,000)	5,160,000	5,800,000	4,100,000
All		5,310,000		
Sedimentation rate				
Male	(5–10 mm.)	11 mm.		
Female	(5–20 mm.)	14 mm.		
Compact cells				
Male	(47%)	46.6%		
Female	(42%)	42.0%		
All		44.3%		
Average total hemoglobin				
Male (100%)	(15.6 gm. per 100 cc.)	99%—15.8 gm. per 100 cc.	118%	90%
Female	(85–90%)	96%—14.1 gm. per 100 cc.	97%	72%
All		97%—14.9 gm. per 100 cc.		
Mean hemoglobin concentration				
Male		32.1%		
Female		32.2%		
All	(33–38%)	32.1%		

Data: Of the 33 members studied, 15 were males and 18 females. The results of the observations are consolidated in Tables I, II, and III.

TABLE II

LEUKOGRAM

		EXPOSED PERSONNEL		
	Normal	Male	Female	All
White blood cell Average total count	(6,000–8,000)	9,900	7,100	8,500
Polymorphonuclears	(64–70%)	55%	50%	52%
Eosinophiles	(2–4%)	2%	2%	2%
Monocytes	(5–7%)	4%	4%	4%
Lymphocytes	(20–25%)	31%	34%	32%

* *Thromboplastic substance* is made up from 100 gm. fresh, ground beef lung which is extracted in the cold for 24–28 hours in 100 cc. saline—stirred frequently. After periodic checks for potency, the mixture is strained, centrifugalized, the liquid decanted off, its pH adjusted (Beckman pH meter) and sealed into 10 cc. vials under negative pressure. These are stored on dry ice. As each vial is removed for use, the potency is tested on known normal blood, the pH again checked and adjusted ($pH_{7.5}$) and the material sealed in capillary tubing in individual units, again kept on dry ice until used.

Prothrombin time, as an indicator of prothrombin concentration is determined by mixing one drop of the thromboplastic substance with four drops of freshly drawn venous blood. Run needle through mixture till the first fibrin filament is formed. This is the end-point. Our thromboplastic substance is adjusted to give a normal time of 25–30 seconds.

Control studies on members of the hospital personnel in other departments did not show these variations.

Many of the radiologic personnel (Table 1) showed high average red blood cell counts, hemoglobin and white blood cell counts, but with reduced neutrophiles and increased lymphocytes (Table II). The consistently lowered neutrophile and consistently higher lymphocyte totals are noteworthy in that others have considered that early radiation effect is best detected by observation of a decrease in the lymphocytes. The repeated subtolerance exposure would appear to induce the reverse.

The coagulogram was altered fairly consistently both as to complete coagulation and prothrombin time, with a high normal fibrin time.

ROYAL VICTORIA HOSPITAL

DEPARTMENT OF MEDICINE

DIVISION OF HAEMATOLOGY

NAME Age Date

WARD Weight Case No.

Sex Dept. No.

Service of Dr.

Clinical Diagnosis

Nature of examination required

Takata Ara

Cephalin Flocculation

Weltam Sero-Flocculation

WBC

Sedimentation rate: 1st hour

2nd hour

Differential count.

Mbl. Pr. Ml. Myel Met. Ml. Stab. Poly. H. Poly. Eosin. Mast. Lymphbl. Lymph. L. Lymph. S. Mono.

COAGULOGRAM

Platelets
Bleeding time
Clot retraction

Prothrombin time
Fibrin time
Complete coagulation
Rumple Leeds test

COMMENTS:

Fig. 2

Similar changes found in any one or more components of the hemograms of ward patients had accountable reasons for the change (e.g., in the group with erythrocytosis one usually found an elevated blood pressure, anoxemia, blood concentration, splenopathy or cardiovascular disease of an

acquired or congenital nature, etc.).

Dicoumarol, salicylate or phenobarbital therapy, hemorrhage, infection, defective diet (particularly in vitamin K content) and liver, gallbladder or gastrointestinal disease will disturb the prothrombin time.

Table III

COAGULOGRAM

	(Normal)	Average	EXPOSED PERSONNEL Maximum	Minimum
Thrombocytes	(200,000)	200,000		
Clot retraction	(present)	(present)		
Bleeding time	(1.5 min.)	1.5 min.		
Fibrin time				
Starting	(1–3 min.)	2 min. 55 sec.		
Male			7 min.	1 min. 20 sec.
Female			7 min. 30 sec.	1 min.
Coagulation complete	(8–10 min.)	13 min.		
Male			36 min.	5 min.
Female			45 min.	8 min.
Prothrombin time	(25–30 sec.)	33 sec		
Male			70 sec.	25 sec.
Female			70 sec.	23 sec.

These disturbing factors were not present in our study group, and on physical examination all were found otherwise normal.

The coagulogram would seem to be a rather delicate indicator of impending disturbance, apparently more sensitive than the cytological elements, save for the two other important observations noted below. Eosinophiles and monocytes were least affected.

The outstanding features of interest in the coagulogram (Table III) are the increase in length of coagulation time as an indicator of fibrin formation and the prolonged prothrombin time as an indicator of diminished prothrombin concentration. This same pattern has since been confirmed in special studies of other individuals.

CONCLUSIONS

1. Systematic observations on the coagulogram, with particular reference to prothrombin concentration, of apparently healthy individuals exposed to repeated minimal amounts of roentgen and radium radiation reveal important warnings of the effect of irradiation.

2. The early effect of repeated subtolerance or threshold doses of x- or gamma radiation on the cytologic elements suggests an irritative reaction as manifested by the mild erythrocytosis and moderate leukocytosis with relative as well as absolute increase in lymphocytes.

3. The present approach in gauging the effects of irradiation is believed to be a more critically potent indicator of exposure than the merely cytologic examination of the blood as in the past.

4. The existence of a large prothrombin reserve is recognized, but it is believed that the deficiency manifestations noted are important evidence that one function of the liver may be affected relative to the degree of its sensitivity to irradiation influence.

5. As a result of our observations, we consider that a lengthening of the prothrombin "time" from a maximum normal of thirty seconds to forty-five seconds warrants a "caution" to the individual and renewed vigilance and discipline in observation of the protective rules in the roentgen-ray and radium laboratories.

If the prothrombin time should be

lengthened to sixty seconds or more (possibly indicative of a reduction in prothrombin concentration of the order of 50 per cent), the individual should be temporarily removed from any exposure area and the deficiency neutralized by every possible means.

If the condition should not be controlled, or progress, a long or permanent separation of the individual from any potential exposure is considered imperative.

6. The possibility is being considered that vitamin K therapy may be a specific for the reduced prothrombin concentration found in connection with irradiation. The degree of deficiency which may respond to such therapy is under investigation, and will be discussed in a later communication.

Royal Victoria Hospital,
Montreal, P.Q.

The cooperation of the personnel of the Department of Radiology as the group studied, and the painstaking labors of the Technical Staff of the Division of Haematology is gratefully acknowledged.

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THE EFFECT OF ROENTGEN THERAPY ON EXPERIMENTAL VIRUS PNEUMONIA*

I. ON FELINE VIRUS PNEUMONIA

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THE high incidence during the past few years of human atypical pneumonia has stimulated numerous studies of the disease especially from the etiological and therapeutic aspects. Because the etiological agent, generally considered to be a virus, has not yet been isolated, treatment has necessarily been nonspecific. Roentgen therapy has been advocated by a number of clinical investigators who reported good results with such treatment. To date no work has been done to determine the effect of irradiation on experimental virus pneumonia. Because of this we investigated the influence of roentgen treatment on virus pneumonia in cats and mice. The present paper is concerned with the study of feline pneumonia produced by the virus originally isolated by Baker.[1,2] The experimental studies with mice are reported in a subsequent paper.[12]

The feline virus (Baker) was chosen as the infectious agent chiefly because it produces in cats a natural disease which in some respects simulates human atypical pneumonia. In both instances the disease is relatively mild, though prolonged, and the mortality rate is low. Baker[1] suggested that the feline virus might be closely related to that responsible for the human pneumonia, but Thomas and Kolb[20] have demonstrated that the virus belongs to the psittacosis-lymphogranuloma group. The latter group, according to Dingle,[11] is relatively unimportant in the etiology of human atypical pneumonia, accounting for a very small percentage of the cases.

EXPERIMENTAL METHODS

Young healthy cats were used. The cat virus was obtained from Dr. J. A. Baker. The virus was passed through mice seventeen times before use. The inoculum consisted of a 1 in 10 suspension of infected mouse lung in Douglas broth. The cats were anesthetized with ether and 0.2 cc. of the virus suspension was placed in the nose with a tuberculin syringe.

Baker showed that there is little correlation between the fever and the severity of the disease, the illness sometimes being afebrile. Thus, although daily rectal temperature readings were made in our experiments the symptoms were used as the chief criterion for the severity of the disease; these were graded daily one plus to six plus. This proved to be a reasonably accurate method because there was a wide range in severity of the symptoms and a decided difference between the acute phase and the convalescent phase of the disease.

The animals were divided into three groups: Group I consisted of 9 cats which served as untreated controls; Group II was made up of 7 cats which received treatment within twenty-four hours after the onset of symptoms; Group III consisted of 6 cats which were treated forty-eight hours after the appearance of symptoms. One cat, No. 23, not included in the above groups, was treated four days prior to the onset of symptoms.

Shortly after the acute phase of the disease had subsided the animals were sacrificed and complete autopsies were performed.

The roentgen rays were generated at 200 kv., 20 ma., and filtered with 0.5 mm. Cu+1 mm. Al (half-value layer, 1.1 mm. Cu). The target-skin distance was 30 cm. and the portal measured 10 by 10 cm. The doses, measured in air without backscatter, consisted of 100 r given once only or 100 r delivered on each of two consecutive days. Some animals were irradiated over the anterior aspect of the thorax and others over the anterior aspect of the abdomen.

RESULTS

1. *Clinical.* All the cats became clinically

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TABLE I

SUMMARY OF EXPERIMENTS ON EFFECT OF ROENTGEN THERAPY ON FELINE VIRUS PNEUMONIA

GROUP I
(Untreated cats)

Cat No.	Area Treated	Dosage	Length in Days of Acute Phase of Illness	*Degree of Pneumonia
1	Untreated	0	5	Moderate
2	Untreated	0	6	Slight
3	Untreated	0	13	Moderate to marked
4	Untreated	0	10	Moderate to marked
5	Untreated	0	14	Slight
6	Untreated	0	11	None
7	Untreated	0	8	Very slight
8	Untreated	0	13	Slight
9	Untreated	0	13	Slight
Mean			10.3	

GROUP II
(Cats treated 24 hours after onset of symptoms)

Cat No.	Area Treated	Dosage	Length of Days in Acute Phase of Illness	Degree of Pneumonia
10	Thorax	100 r once	5	Slight
11	Thorax	100 r once	4	Very slight
12	Thorax	100 r once	5	Moderate
13	Thorax	100 r once	5	Marked
14	Thorax	100 r twice	4	Slight
15	Abdomen	100 r once	7	Slight
16	Abdomen	100 r twice	5	Slight to moderate
Mean			5	

GROUP III
(Cats treated 48 hours after onset of symptoms)

Cat No.	Area Treated	Dosage	Length in Days in Acute Phase of Illness	Degree of Pneumonia
17	Thorax	100 r once	7	Moderate
18	Thorax	100 r once	7	Slight
19	Thorax	100 r once	7	Slight to moderate
20	Thorax	100 r once	6	Slight
21	Thorax	100 r twice	10	Moderate
22	Thorax	100 r twice	8	Moderate
Mean			7.5	

* While the degree of pneumonia varied, that of the conjunctivitis and the rhinitis was equally severe in all cats.

ill. The clinical picture was similar to that described by Baker.[2] The average duration of the incubation period was nine days. The disease was characterized by photophobia, lacrimation, sneezing, sniffling, coughing, anorexia, and lassitude. Most of the cats showed a brief prodromal stage of slight lacrimation and photophobia followed by a brief remission, shortly after which definite, progressive symptoms developed. As previously mentioned the temperature was variable, frequently being normal at the height of the symptoms. In the control cats (Group I) the average length of the acute phase of the disease was 10.3 days with some variation from the mean (Table 1).

The cats that received roentgen treatment within twenty-four hours of the development of symptoms (Group II) were acutely ill for an average of five days, with but little variation from the mean (Table 1). Some animals of this group received one treatment to the thorax, some two successive treatments to the thorax, while others received either one or two treatments to the abdomen. In spite of this variation in the site treated, all cats in this group were benefited. A statistical analysis showed that the difference in the duration of the disease in Groups I and II was highly significant.

The animals in Group III, treated with roentgen rays forty-eight hours after the onset of symptoms were acutely ill for an average of 7.5 days as compared with 10.3 days for the controls. This difference, however, was found to be insignificant on statistical analysis.

One cat that received 100 r to the thorax four days prior to the development of symptoms was sick for only three days. This animal was not included in the test groups because it was the only one so treated.

2. *Anatomical.* The autopsies were performed shortly after the acute phase of the disease had ended, so that only the convalescent phase of the disease was represented in the tissues. The main lesions were in the conjunctiva, the nose and the lungs; lesions of less importance occurred in the lacrimal glands, the trachea and the larynx. Of 23 cats inoculated, all had conjunctivitis and rhinitis and 20 had definite pneumonia; 1 cat showed no pulmonary lesions and 2 other cats had only very slight focal pneumonia.

The nasal mucous membrane suffered the greatest damage, showing destruction of the respiratory epithelium with a marked inflammatory response. The anterior portion of the nasal cavity lined by squamous epithelium escaped injury, and the posterior portion lined by olfactory epithelium was only slightly involved. The conjunctiva showed changes comparable to those seen in the nose, and in some cats there was also slight focal round cell infiltration of the lacrimal glands. The larynx and trachea in some instances were slightly inflamed, the cellular infiltration occurring mainly in the submucosal glands. The lungs showed a slight to moderate degree of interstitial inflammation, the bronchial epithelium being relatively uninjured.

No essential differences between the tissues of the control and test groups, either in the degree or extent of the inflammatory reaction, were detected histologically.

DISCUSSION

A number of recent clinical reports state that roentgen therapy is of value in the treatment of human atypical pneumonia. Oppenheimer[16,17] stressed the fact that small doses to the thorax resulted in prompt amelioration of the symptoms, without, however, immediate resolution of the pneumonia. Correll and Cowan[8] reported that roentgen therapy shortened the course of the illness considerably, and Schmitz[19] in his comprehensive review referred to frequent use of roentgen therapy.

The results of irradiation of our experimental animals were similar to those observed in human atypical pneumonia. Roentgen treatment within twenty-four hours after the onset of symptoms in the

animals definitely shortened the acute phase of the illness. The discrepancy between the clinical and anatomical findings is not surprising, since in many infectious processes clinical cure precedes the complete healing of the tissues.

The manner in which roentgen irradiation favorably influences infectious processes remains obscure. Practically all experimental studies have been concerned with bacterial diseases. Many of these are of questionable value because the doses used were far in excess of those we now know to be effective. Clinical experience has taught that small doses are essential in the treatment of infections, and in recent years this has been corroborated experimentally.[15]

Experiments dealing with the influence of roentgen rays upon the infectious agent itself have shown that huge doses are required to destroy bacteria. Doses found by Korb[14] to be lethal for bacteria are no longer employed in treating infections; it is doubtful, therefore, that the favorable action of roentgen rays results from any direct effect upon the organism.

Irradiation is capable of altering complex protein molecules, so affecting the cell permeability that a disturbance of fluid balance occurs.[7] There is as yet little evidence that this feature is important in the treatment of infections. Roentgen rays are known to alter the albumin-globulin ratio in the tissues, producing a local increase in the globulin fraction. Since it is now apparent that antibodies are specific globulins, it has been suggested that roentgen therapy may make a greater quantity of globulin available for antibody production.[18]

Roentgen rays in certain doses produce dilatation of the smaller vessels. Borak[5] and others assert that the increased supply of blood to the infected area results in a local increase in antibodies and phagocytes, and also removes local toxins. This theory seems to disregard the more general effects of irradiation.

Desjardins[9,10] has for many years suggested that the beneficial effects of roentgen irradiation on infections are due to the release of antibodies resulting from the destruction of leukocytes at the site of treatment.

Recently Bisgard and his co-workers[3,4] demonstrated that roentgen treatment of rabbits forty-eight hours prior to the injection of lethal bacterial toxins significantly lowered the mortality rate. They concluded that the roentgen irradiation produced a nonspecific antitoxin. It appears to us more likely that the treatment in some way enables the animals to react quickly and effectively in a specific fashion. A large number of substances can favorably affect the antibody-producing mechanism[6] in a nonspecific manner; perhaps roentgen rays can be added to this list. Burnet[6] has also shown that under certain conditions the maximum antibody response to a secondary antigenic stimulus takes place forty-eight hours later; hence, the forty-eight hour latent period described by Bisgard and his co-workers may represent the interval necessary for the activation by roentgen irradiation of the antibody-producing mechanism.

In keeping with this forty-eight hour period of response, Glenn[13] demonstrated that rabbits show a significant rise in the phagocytic index after roentgen treatment. This effect reached its peak in forty-eight hours; the indices returned to normal within a week. This indicates that roentgen irradiation can modify at least one phase of the antibody response of normal rabbits.

The observations just discussed stress both local and general effects of roentgen irradiation upon infection. While the early local effects are important, general effects such as stimulation of the reticuloendothelial system resulting in increased phagocytosis and antibody production may be more significant.

It is obvious that more work must be done to elucidate the mechanism by which roentgen irradiation increases the resistance of the host to infection. Nevertheless, our experiments indicate that the early use of

roentgen therapy is valuable in the treatment of feline virus pneumonia, significantly shortening the duration of the acute phase of the disease.

SUMMARY AND CONCLUSIONS

A study of the effects of roentgen therapy in feline virus pneumonia was made. Infected control animals were acutely ill for an average of 10.3 days, while infected animals treated with roentgen rays twenty-four hours after onset of symptoms were sick only five days. Similar therapy instituted forty-eight hours after the initial appearance of symptoms had no appreciable influence upon the course of the disease. No differences were seen in the tissues of the control and test animals.

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THE EFFECT OF ROENTGEN THERAPY ON EXPERIMENTAL VIRUS PNEUMONIA*

II. ON PNEUMONIA PRODUCED IN WHITE MICE BY SWINE INFLUENZA VIRUS

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IN A previously reported experiment,[1] we found that roentgen therapy instituted twenty-four hours after onset of symptoms shortened the acute phase of feline virus pneumonia from ten to five days. Having thus demonstrated that this form of treatment is of value in a relatively mild form of virus pneumonia, we have now investigated the effect of such therapy in a severe virus pneumonia with a high mortality rate. For this purpose we have used white mice infected with swine influenza virus. The pneumonia produced in mice by this virus kills the animals within a few days when the virus is used in sufficiently high concentration.

MATERIALS AND METHODS

White mice about three to five weeks old were used. The strain of swine influenza virus employed was obtained from Dr. J. W. Beard. The inoculum consisted of a 1 in 100 suspension of infected mouse lung in Douglas broth. Five hundredths cubic centimeter of the inoculum was dropped on the noses of the mice with a tuberculin syringe while the animals were under light ether anesthesia.

The mice were treated in their cages, the entire surface of the body of each animal being exposed to irradiation. The cages were wooden and measured 8 by 13 inches; the tops of the cages were removed prior to treatment. The roentgen rays were generated at 200 kv. and 20 ma., filtered with 0.5 mm. Cu+1 mm. Al; the target-skin distance was 80 cm. and the portal measured 30 by 30 cm. The dosage varied from 5 to 200 r. All measurements of doses were air readings without backscatter.

Three experiments were done including three control and ten test groups. In all but two test groups—these were treated forty-eight hours before inoculation—treatment was instituted twenty-four hours after inoculation of the virus, because by this time the pneumonia is well established.[4] The experiments were allowed to run for ten days, since almost all deaths from this disease occur within this period. On the tenth day the surviving mice were killed with ether and the lungs examined. All the mice developed pneumonia except three—one in Group 5, one in Group 6, and one in Group 8.

Experiment I. In this experiment there were four groups of 25 mice each: Group 1 received no treatment; Group 2 received 5 r twenty-four hours after inoculation of the virus; Group 3 received 5 r and 10 r twenty-four and forty-eight hours after inoculation respectively; Group 4 received 5 r, 10 r, and 15 r twenty-four, forty-eight, and seventy-two hours after inoculation respectively.

Table 1 shows the results of this experiment; these are recorded as the total number of mice which were dead by the end of each day of the experiment. The number of mice which had died in each group by the end of the tenth day was as follows: 22 in Group 1, 17 in Group 2, 24 in Group 3, and 23 in Group 4. A statistical analysis, using the chi-square method, shows that the only significant difference in the mortality between the control and the test groups occurred on the sixth and seventh days in Group 2. By the tenth day, however, the difference between the control group and Group 2 was found to be not significant.

Experiment II. In view of the fact that the results of Experiment 1 suggested that treatment with 5 r may have reduced the mortality rate, the experiment using this dosage was repeated. In addition, other groups were treated with larger doses of roentgen rays. In this experiment there were four groups (numbers 5 to 8 inclusive) of 18 mice each: Group 5 received no treatment, while Groups 6, 7, and 8 were treated twenty-four hours after inoculation of the virus with 5 r, 50 r, and 100 r respectively.

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TABLE I

SUMMARY OF EXPERIMENTS ON EFFECT OF ROENTGEN THERAPY ON PNEUMONIA PRODUCED IN MICE BY SWINE INFLUENZA VIRUS

(The figures represent the daily cumulative mortality of the respective groups of mice)

Experiment I
(25 mice per group)

Number of days after inoculation of virus	1	2	3	4	5	6	7	8	9	10
Group 1 Untreated	0	0	2	9	13	21	22	22	22	22
Group 2 5 r 24 hours after inoculation	0	0	0	5	10	14	15	17	17	17
Group 3 5 r and 10 r 24 and 48 hours after inoculation respectively	0	0	1	6	13	22	23	23	24	24
Group 4 5 r, 10 r and 15 r 24, 48 and 72 hours after inoculation respectively	0	0	2	10	13	17	21	22	23	23

Experiment II
(18 mice per group)

Number of days after inoculation of virus	1	2	3	4	5	6	7	8	9	10
Group 5 Untreated	0	0	0	1	2	5	8	12	14	15
Group 6 5 r 24 hours after inoculation	0	0	0	1	2	3	7	13	13	13
Group 7 50 r 24 hours after inoculation	0	0	0	0	2	5	10	13	13	14
Group 8 100 r 24 hours after inoculation	0	0	0	2	2	7	8	12	12	12

Experiment III
(16 mice per group)

Number of days after inoculation of virus	1	2	3	4	5	6	7	8	9	10
Group 9 Untreated	0	0	3	9	15	15	15	15	15	15
Group 10 100 r 24 hours after inoculation	0	0	0	6	13	13	14	14	14	14
Group 11 200 r 24 hours after inoculation	0	0	1	6	12	14	14	14	14	14
Group 12 5 r 48 hours before inoculation	0	0	1	5	11	12	13	14	14	14
Group 13 100 r 48 hours before inoculation	0	0	0	3	7	9	10	10	10	10

The results, which appear in Table 1, show that there is no significant difference between the mortality of the control and test groups for each of the ten days. In the untreated group, 15 of 18 mice had died by the end of the tenth day, while in Groups 6, 7, and 8 the number of mice that had died was 13, 14, and 12 respectively.

Experiment III. Since Group 8 had the lowest mortality rate in Experiment II, the experiment using this dosage (100 r) was repeated. In addition, two groups were treated with roentgen rays forty-eight hours *before* inoculation with the virus, since such treatment has been shown to increase resistance to a lethal dose of bacterial toxins in rabbits.[3]

There were five groups (numbers 9 to 13 inclusive) of 16 mice each: Group 9 received no treatment; Groups 10 and 11 were treated twenty-four hours *after* inoculation of the virus with 100 r and 200 r respectively; Groups 12 and 13 were treated with 5 r and 100 r respectively forty-eight hours *before* inoculation of the virus.

The results are shown in Table 1. Of the four test groups only Group 13 showed a significant decrease in the mortality rate. By the tenth day 15 of the 16 mice were dead in the control group and only 10 mice were dead in the group treated with 100 r forty-eight hours before inoculation —a reduction in the mortality by about one-third. Statistical analysis, using the chi-square method, of the daily cumulative mortality figures showed that the differences between these two groups were significant for days four to ten inclusive, the difference on the fifth day being highly significant.

DISCUSSION

These experiments show that roentgen therapy over a wide range of dosage (from 5 r to 200 r) has no effect upon the mortality rate of pneumonia produced in mice by swine influenza virus when this therapy is given twenty-four hours after infection. This negative finding stands in sharp contrast to the positive result obtained with similar therapy in the virus pneumonia of cats, a disease of negligible mortality. There may be several factors involved in this difference in results. Probably the most important is the difference in the severity of the two diseases. In the virus pneumonia produced in mice the disease is well established at twenty-four hours, at which time most of the test groups were treated. Since there is evidence which indicates that the effect of roentgen irradiation is at its height forty-eight hours after treatment,[2,5] this maximum effect would occur three days after inoculation of the virus, at which time severe damage had already occurred, even to the point of producing death in some mice.

That roentgen therapy does favorably influence the course of swine influenza virus pneumonia is demonstrated in Experiment III, by the significant decrease in mortality which occurred in the group of mice treated with 100 r forty-eight hours before inoculation of the virus. This protective effect is lost, however, when therapy is administered *after* the onset of the infection, probably because the maximum effect is produced too late in the course of so violent a disease.

Several theories have been proposed to explain the beneficial effect of roentgen irradiation on infections. These have been discussed in our previous paper.[1] It seems that the maximum effect occurs about forty-eight hours after treatment. This lag suggests that a mechanism is at play which requires the multiplication of living agents. It appears to us that roentgen irradiation activates the reticuloendothelial system, probably causing a multiplication of reticuloendothelial cells, so that the increased number of these elements makes for better phagocytosis and antibody production, thereby increasing resistance to infection. This hypothesis is consistent with Burnet's theory of antibody production.[3] The matter is speculative, and obviously further experiments are necessary for clarification of the mechanism involved.

SUMMARY

Roentgen therapy instituted twenty-four hours *after* inoculation of mice with swine influenza virus has no effect upon the mortality of this disease. Similar therapy given forty-eight hours *before* infection of

the animals produces a significant decrease in the mortality, about one-third.

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Forty-seventh Annual Meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Sept. 17–20, 1946.

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Twenty-eighth Annual Meeting: San Francisco, Calif., June 28–29, 1946.

EDITORIALS

AEROTITIS AND ITS PREVENTION BY THE USE OF RADIUM

THE earliest attempts to study the effect of a sudden change of pressure on the ventilation of the middle ear during flight were made in World War I. Scott[1] in February, 1918, was assigned to the B.E.F. in France "to investigate certain questions connected with the special disorders of flying." In a period of four months he examined upwards of 300 flying officers, more than one-half of whom were affected with one or more auditory symptoms such as pain in the ears, deafness, headache, vertigo, and nausea. It was found that these symptoms were the result of inefficient eustachian tubes, which would not permit an airman to correctly regulate and equalize the changes of atmospheric pressure from high to low altitudes, and vice versa. An examination of the ears immediately after landing revealed that the fundus was bright red owing to distention of the blood vessels in the tympanic membrane and mucosa of the middle ear. In extreme cases there was an invagination of the tympanic membrane into the tympanum and occasionally globules of mucus could be observed through the invaginated drumhead within the tympanic cavity. With the relatively small speed of the fastest planes available at that time and with a maximum flying altitude of 20,000 feet it was often possible to prevent these symptoms by teaching the airmen auto-inflation by swallowing, yawning or Valsalva's method which they practiced when starting to dive and repeated at every 1,000 and 1,500 feet until landing safely. However, during more prolonged flights, at a high altitude or in strenuous aerial combats, such simple procedures failed to open up the lumen of the eustachian tubes and due to lack of other remedies the symptoms continued to last for hours, days or weeks, seriously impairing the utility of the person to the Service.

In 1937, Armstrong and Heim[2] made a very comprehensive study of the physiology of the eustachian tubes under marked variations of atmospheric pressure through ranges of from 760 to 141 mm. of mercury (0 to 40,000 ft. altitude). They found that opening of the eustachian tubes by voluntary effort equalized the air pressure but when a negative pressure of from 80 to 90 mm. of mercury developed in the tympanic cavity further voluntary opening became impossible and no equalization of the air pressure could be obtained. This then led to discomfort, pain, tinnitus and deafness. The phenomenon occurred so regularly that Armstrong and Heim thought that a new clinical entity should be created. They suggested the name of aero-otitis media and defined the entity as an acute or chronic traumatic inflammation of the middle ear caused by a pressure difference between the tympanic cavity and that of the surrounding atmosphere commonly occurring during changes of altitude in airplane flights. The two main causes accounting for the lack of equalization of the air pressure were the failure to open the eustachian tube voluntarily when necessary and the inability to open it. The first was most often due to inexperience, to falling asleep or to being under the influence of analgesics. The second included a variety of possibilities, the most important among them being acute or chronic infection of the

[1] Scott, Sydney. The ear in relation to certain disabilities in flying. *J. Laryngol., Rhinol. & Otol.*, 1920, *35*, 225–243.

[2] Armstrong, H. G., and Heim, J. W. Effect of flight on the middle ear. *J. Am. M. Ass.*, 1937, *109*, 417–421.

upper respiratory tract and accessory sinuses, inflammatory conditions of the eustachian tube or middle ear and, above all, enlargement of the pharyngeal and tubal tonsil.

In 1944, Larkin[3] studied the mechanism of trauma in aerotitis by means of roentgenography. He devised methods which permitted the visualization of the extermal meatus, the shifting of the tympanic membrane as shown by the position assumed by the auditory ossicles, the presence of fluid in and about the tympanic cavity and the patency of the eustachian tube. With the aid of these methods he found that aerotitis is characterized by blurring of the ossicles and clouding of the cells of the petrous bone and of the mastoid process due to hydrops ex vacuo. The increased negative pressure changes the osmotic conditions with the result that fluid oozes from the mucosa lining the air cells and covering the auditory ossicles. In severe cases the accumulation of fluid in the tympanic cavity may be so pronounced that on otoscopic examination a clear fluid line becomes visible behind the drum. If the pressure gradient exceeds half an atmosphere the tympanic membrane ruptures. It was also possible to demonstrate on the roentgenograms a blockage of the eustachian tube, usually at the pharyngeal end, and a marked shrinkage of the mucosa of the posterior oral pharynx and of the pharyngeal ostium of the eustachian tube following the application of 10 per cent cocaine for therapeutic purposes.

It appears from all these considerations that the frequency of aerotitis in airmen must be the result of a rather common predisposing cause. The pioneer work of Crowe and his associates[4] has pointed in the direction of the lymphoid hyperplasia in and about the pharyngeal ostium of the eustachian tube which from childhood so often interferes with the proper ventilation of the middle ear, leading to a slowly progressive deafness in later life. Similarly, the presence of excessive amounts of lymphoid deposits around the pharyngeal end of the eustachian tubes, although quite harmless under ordinary circumstances, might interfere with the good equalization of the pressure in airmen during strenuous flights, gradually blocking the eustachian tubes and thus giving rise to aerotitis.

In seeking some remedy for the deafness in children, Crowe and his associates soon found that the destruction of the excessive lymphoid tissue by a source of locally applied radium was followed by improvement or complete clearing up of the deafness in many instances. For various reasons they used the beta rays of very powerful radon bombs, but later other investigators[5] obtained equally favorable results with the gamma rays.

In World War II the amazing technical improvements realized in the construction of all types of flying apparatus have placed an ever increasing strain on the ability of the average airman to ventilate his middle ear during flight. Because of this, aerotitis became a rather common occurrence, especially in those theatres where climatic conditions were responsible for recurring colds leading to marked lymphoid hyperplasia of the posterior oral pharynx and around the pharyngeal ostium of the eustachian tubes. In fact, as one of the Air Force Theatre Surgeons reported in 1944, aerotitis in some units interfered with the availability for combat duty of the airmen a third of the time.

In order to correct this situation, the Air Surgeon in May, 1944, organized the so-called Army Air Forces Aerotitis Control Program. Ten otologists were called together and specially trained at Johns Hopkins University, under the direction of Crowe, in nasopharyngoscopy and radium irradiation of the lymphoid hyperplasia of

[3] Larkin, J. C. Aero-otitis media; roentgenologic study. Am. J. Roentgenol. & Rad. Therapy, 1944, *51*, 178–185.

[4] Crowe, S. J., and Baylor, J. W. Prevention of deafness. *J. Am. M. Ass.*, 1939, *112*, 585–590. Crowe, S. J., and Burnam, C. F. Recognition, treatment and prevention of hearing impairment in children. *Ann. Otol., Rhin. & Laryng.*, 1941, *50*, 15–31.

[5] Fricke, R. E., and Brown, H. A. Radium treatment of nasopharyngeal lymphoid hypertrophy. *South. M. J.*, 1944, *37*, 399–402.

the eustachian tubes as a control measure of aerotitis. These physicians were then sent to various Air Forces where they carried out the program along identical lines, allowing only slight variations dependent upon local conditions. Recently their experience was published in an excellent combined report.[6]

Five Air Forces participated in the program. The First and Third Air Forces were located in the United States, the Eighth, Twelfth and Fifteenth covered the European and Mediterranean Theatres of Operation. The program in the First Air Force was conducted at three heavy bomber training bases and one staging base. An Irradiation Clinic was established at Westover Field, Massachusetts, and another at Mitchell Field, New York. The Third Air Force had one Irradiation Clinic at Drew Field, Tampa, Florida. In the Theatres of Operation the medical officers entrusted with the program worked in the field. The Eighth Air Force had three Air Divisions, and a medical officer was assigned to each Division, the examinations and irradiation being carried out at the dispensaries on the base of each Division. A tour of all bases was made once a month. The necessary equipment was carried from base to base by jeeps, ambulances, reconnaissance cars, trucks, mail carriers and airplanes. This Air Force operated from England. The irradiation project of the Twelfth Air Force was conducted by one medical officer. The mission at the time of the study called for rapid movements over widely scattered areas. The travel was by all types of aircraft and land vehicles. The medical officer followed the flying fighting personnel from point to point over the entire length of Corsica, throughout northern Italy, across France and into Germany. The examinations were made and the necessary treatments given in tents, churches, barrooms, messes, hotels, palaces, ballrooms, convents, dispensaries and in hospitals. The Fifteenth Air Force likewise had only one medical officer. The Irradiation Clinic travelled between bomb groups by jeep and trailer. The units were situated within a radius of fifty miles excepting one which was two hundred miles away. The visits here, too, were made once a month.

As one may note, the program was outlined in such a manner that every possible climatic variation was covered. Due consideration was also given to all types of operational influences. In the Forces stationed in the United States it was often found impossible to accurately differentiate between the lack of experience of the men to properly ventilate their middle ear and true aerotitis, and therefore selection of treatment was based upon the presence of lymphoid hyperplasia in and about the eustachian tube predisposing to aerotitis. At Westover Field a group of 922 men with clear eustachian orifices were also observed for about six months as a control to a group of 778 men with lymphoid hyperplasia irradiated prophylactically. In the Forces located in the combat zones, men with definite aerotitis or having difficulty in clearing their ears were chosen almost exclusively for treatment. The only other control study was made at the Eighth Air Force in England where a group of 66 men with aerotitis due to lymphoid hyperplasia, who were not treated, were observed for a few months as a control of a similar group treated by irradiation.

To better evaluate the results, standard methods of history taking, of examination, of interpretation of findings and of treatment were applied. For nasopharyngoscopy the nose was sprayed lightly with a 5 per cent butyn solution and then a cotton swab moistened with 20 per cent cocaine solution was passed along the floor of the nose. After a few minutes the nasopharyngoscope was introduced and the entire nasopharynx surveyed. It was not so much the amount

[6] The use of radium in the aerotitis control program of the Army Air Forces. First Air Force: Hendricks, John E., Lieberman, Alfred T., Lyman, Edward, Magnuson, Paul L., McMurray, John, and Weymuller, Ernest A.; Third Air Force: Earl, Donald H., Glauber, Jerome J., and Smith, John W.; Eighth Air Force: Collins, Braswell E., Eschenbrenner, John W., Jr., and Lyle, Philip L.; Twelfth Air Force: Mikell, John S.; and Fifteenth Air Force: Trapasso, Tony J. *Ann. Otol., Rhin. & Laryng.*, 1945, *54*, 649–724.

as the location of the lymphatic hyperplasia that counted. Small infected nodes in the fossa of Rosenmüller, in the area between the eustachian tube and the middle turbinate, and especially in or around the pharyngeal ostium of the eustachian tube, were found to be of particular importance. The treatment was carried out by placing radium directly against the areas of lymphoid hyperplasia. Two applicators were used simultaneously, one on each side. The applicators consisted of a radium-containing chamber brazed to a wire handle so that it could not break and be swallowed or aspirated. The chamber was made of monel metal, 2 cm. long, had an outside diameter of 2.3 mm., an inside diameter of 1.7 mm., a wall thickness of 0.3 mm. and contained approximately 50 mg. of radium sulphate. This filtration permitted an emission of approximately 30 per cent beta rays and 70 per cent gamma rays. The applicators were inserted into the nasopharynx with the patient lying on a cot or bed, and left in situ for 6.6 minutes in the beginning and 8.5 minutes later. The dose thus amounted to 1 gm. 20 seconds and 1 gm. 25 seconds respectively. The increase in dose was found to lead to better results and yet no untoward reactions were observed. Whenever possible, three radium applications were made at intervals of twenty-five to thirty days. No treatment was undertaken in the presence of an acute upper respiratory infection. In case of a subacute nasopharyngitis only one-half of the dose was given first and the other half five days later. Because of rapid displacement in the combat zones and the necessity of fulfilling certain training schedules at the bases in the United States, many airmen received only one or two radium applications. In all Irradiation Clinics rigid protective measures were observed to prevent injury to the personnel. The radium treatment rooms were at a distance of at least 20 feet from the examining rooms and the actual handling of the applicators was carried out as speedily as possible. After removal from the nose, the applicators were rinsed, rubbed against a soft brush fastened to the sink, rinsed again and then placed in the alcohol tubes in a thick lead container. Special provisions were made not to damage or break the radium chambers during transport since the escape of radon would render them useless.

The Aerotitis Control Program extended over a period of twelve months. During this time a total of 14,345 men were examined in the participating five Air Forces, and 6,881 men were selected for treatment. The number of the individual treatments amounted to 14,045, without a single case of untoward effect. A very small proportion of the men complained of a slight fullness or mild sore throat after treatment.

Because of the influence of extreme variations in the climate and the constant shifting of the men, it was found difficult to accurately evaluate the final results. In the five Air Forces together, only 636 men were available for examination thirty days after their second or third treatments. Of these, 74 per cent showed subjective and 89 per cent objective improvement, always more marked after the third treatment. In the group of 778 men irradiated prophylactically at Westover Field the incidence of aerotitis was reduced from twice that in the control group of 922 men with normal eustachian orifices to a level almost identical with the control group. The principal causes of failure were large adenoids, nasal allergy, chronic sinusitis and psychologic reactions.

Similar observations were made by Fowler[7] who while assigned to an Army General hospital in England used radon obtained from British sources. He reported in 1944 on a group of Air Force personnel who were afflicted by recurrent aerotitis and who responded well to irradiation of the lymphoid hyperplasia around the eustachian tubes with the radon applicators. Later he changed to gamma-ray applicators by using 50 mg. of radium, filtered

[7] Fowler, E. P., Jr. Use of radon to prevent otitis media due to hyperplasia of lymphoid tissue and barotrauma (aero-otitis) *Arch. Otolaryng.*, 1944, *40*, 402–405.

with 0.5 mm. of platinum, for one hour (50 mg-hr.) to each side.

In a recent very comprehensive article, Fowler[8] published the results in 80 airmen who had been treated with radon or radium. Of these, 66 received two or more treatments and were followed up. In 69 per cent there was full recovery. To rule out the possibility of a psychic effect Fowler decided to use dummy capsules in a certain number of airmen for control. Of 34 alternate patients 17 were treated with 50 mg-hr. of radium to each side and 17 with the dummy capsules. Only one of the 17 treated with the placebos returned to flying duty without symptoms, whereas of the 17 alternate airmen who received the active capsules 13 returned to full flying duty.

One may draw the general conclusion from these very interesting studies that the destruction of lymphoid hyperplasia in and about the pharyngeal ostium of the eustachian tubes by the local use of radium eliminates a major cause of aerotitis. Such a procedure is easy to carry out and is devoid of any undesirable effect.

T. Leucutia

[8] Fowler, E. P., Jr. Irradiation of the eustachian tube. *Arch. Otolaryng.*, 1946, *43*, 1–11.

LLOYD BRYAN
1884–1945

DR. LLOYD BRYAN, one of California's best known radiologists, died on December 21, 1945, after a protracted illness. He had been a member of the American Roentgen Ray Society for almost twenty-eight years.

Dr. Bryan was born in Fortuna, California, in 1884. He was graduated with the degree B.S. at the University of California in 1909, and M.D. in 1911. After a year's internship at the University Hospital, he took up private practice in Eureka, California, and practiced general medicine there for four years. He commenced his

radiological career in 1917 with the late Dr. Howard Ruggles in San Francisco, and was soon appointed visiting radiologist to many local hospitals, notably the Dante, Franklin, Mount Zion and San Francisco City and County Hospitals. He was eventually appointed Associate Professor of Roentgenology at the University of California Medical School.

Lloyd Bryan was possessed of an extraordinarily warm personality, and quickly impressed colleagues and students with his sympathetic understanding, as well as his deep knowledge of his chosen specialty. He assisted many younger physicians in getting started in their own professional careers, both inside and outside of his particular field. Like so many other early workers, he sustained irradiation dermatitis of his hands in the early twenties and this caused him no little discomfort in his later life. Despite painful and at times crippling spinal arthritis, as well as a severe chronic gastric lesion, and several coronary occlusive episodes, he maintained a cheerful demeanor at all times, and was a source of great inspiration to those who knew his difficulties.

Dr. Bryan was the author of numerous articles, several of which were published in this JOURNAL, the earliest being one on the important subject of "Roentgen Pleuritis" in 1918. He was a member of the American Roentgen Ray Society, the American College of Radiology, and the Radiological Society of North America—being president of the latter Society in 1935; he was certified by the American Board of Radiology in the preceding year. He was also a member of the Pacific Roentgen Society, the California Medical Association and the American Medical Association. He belonged to many social organizations in the city, notably the Family Club and the Commonwealth Club.

In 1912 he married Miss Alice Downes in San Francisco. He is survived, besides his wife, by two children—Dr. John Ruggles Bryan and Mrs. John Martin Hanlon.

L. H. GARLAND

ABRAHAM STRAUSS
1887–1946

DR. ABRAHAM STRAUSS died suddenly at his home in Cleveland, Ohio, on January 30, 1946. On the previous day he had been in apparently good health, carrying on his work at hospital and office.

Dr. Strauss was born in 1887 in Pawtucket, Rhode Island. He was graduated from Harvard University in 1908 and from Johns Hopkins Medical School in 1912. He had postgraduate surgical training at Mount Sinai Hospital in New York and then came to Cleveland and in 1916 joined the surgical staff of the newly founded Mount Sinai Hospital in that city. From

1940 until the time of his death he was chief of the department of surgery at that hospital.

He was a diplomate of the American Board of Surgery and of the American Board of Radiology and a fellow of the American College of Surgeons. He was a member of numerous medical societies including the Cleveland Radiological Society, the American Radium Society, and the Radiological Society of North America. He was a trustee of the Cleveland Health Museum and of the Cleveland Medical Library, having been elected treasurer of the latter organization a few days before his death.

Dr. Strauss carried on an active surgical practice but he always had a special interest in tumors. For over twenty-five years he had used radium with unusual technical skill. He was largely responsible for the formation of the Tumor Clinic at Mount Sinai Hospital, where his broad surgical experience and his knowledge of radiation therapy made him a most valuable consultant.

During World War I Dr. Strauss served as Captain in the Medical Corps with the British Expeditionary Forces, and was taken prisoner by the Germans.

He is survived by his wife, Mrs. Marion Halle Strauss, and by three daughters.

Dr. Strauss had a wide knowledge of surgery which he applied with great technical skill. The younger surgeons associated with him will long remember his patience and consideration. His patients will long remember his kindness and genuine concern for their welfare.

Lawrence A. Pomeroy

RESOLUTION

The members of the Cleveland Radiological Society were shocked by the news of the sudden death of Abraham Strauss.

Dr. Strauss, a surgeon interested in radium therapy, was a charter member of this Society. As his surgical practice and its responsibilities increased he retained his interest in radium. As Chief of Surgery at Mt. Sinai Hospital he had a broad view of the treatment of tumors by surgery and by irradiation. He will always be remembered for his kindness to his patients, for his encouragement of younger doctors as well as for his broad knowledge of surgery and its skillful technical application.

The members of this Society wish to express to the family of Dr. Strauss their feeling of great personal loss and direct that this expression of their feelings be inscribed on the records of the organization.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Sept. 17–20, 1946.

American College of Radiology
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago.

Section on Radiology, American Medical Association
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio. Annual meeting: San Francisco, Calif., July 1–5, 1946.

American Radium Society
Secretary, Dr. E. H. Skinner, 1532 Professional Bldg., Kansas City, Mo. Annual meeting: San Francisco, Calif., June 28–29, 1946.

Arkansas Radiological Society
Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1946, to be announced.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Section on Radiology, California Medical Association
Secretary, Dr. Gordon G. King, 3700 California St., San Francisco 18, Calif.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

Radiological Section, Los Angeles Co. Med. Assn.
Secretary, Dr. Roy W. Johnson, 1407 S. Hope St., Los Angeles, Calif. Meets on second Wednesday of each month at the County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N.Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

Chicago Roentgen Society
Secretary, Dr. F. H. Squire, 1754 W. Congress St., Chicago 12, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. Carroll C. Dundon, 11311 Shaker Blvd., Cleveland, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Denver Radiological Club
Secretary, Dr. A. Page Jackson, Jr., 1612 Tremont Place, Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida Radiological Society
Secretary, Dr. J. F. Pitman, Blanch Hotel Annex, Lake City, Fla. Meetings in May and November.

Georgia Radiological Society
Secretary, Dr. James J. Clark, 478 Peachtree St., Atlanta, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meets annually second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Michigan Association of Roentgenologists
Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. Annette T. Stenstrom, 1218 Medical Arts Bldg., Minneapolis, Minn. One meeting a year at time of Minnesota State Medical Association.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

New Hampshire Roentgen Ray Society
Secretary, Dr. Richard C. Batt, Berlin, N. H. Four meetings a year.

Radiological Society of New Jersey
Secretary, Dr. H. R. Brindle, 501 Grand Ave., Asbury Pk. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

New York Roentgen Society
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting, Carolina Hotel, Pinehurst, N. C., May 1, 1946.

*** Secretaries of Societies not here listed are requested to send the necessary information to the Editor.**

North Dakota Radiological Society
Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

Ohio Radiological Society
Secretary, Dr. Henry Snow, 1061 Reibold Bldg., Dayton, Ohio. Meets during annual meeting of Ohio State Medical Association.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport. Annual meeting, Berkshire Hotel, Reading, Pa., May 17–18, 1946.

Philadelphia Roentgen Ray Society
Secretary, Dr. C. L. Stewart, Jefferson Hospital. Meets first Thursday of each month, October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. L. M. J. Freedman, 4800 Friendship Ave. Meets 6:30 P.M. at The Ruskin on second Wednesday, each month, October to May inclusive.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Murray P. George, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary Dr. A. M. Popma, 220 N. First St., Boise, Idaho.

St. Louis Society of Radiologists
Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September.

San Diego Roentgen Society
Secretary, Dr. Henry L. Jaffe, Naval Hospital, Balboa Park, San Diego, Calif. Meets monthly on first Wednesday at dinner.

San Francisco Radiological Society
Secretary, Dr. Joseph Levitin, 516 Sutter St., San Francisco 2, Calif. Meets monthly on the third Thursday at 7:45 P.M., first six months of the year at Lane Hall, Stanford University Hospital, and second six months at Toland Hall, University of California Hospital.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. E. L. Flanagan, 116 E. Franklin St., Richmond, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Thomas Carlile, 1115 Terry St., Seattle. Meets fourth Monday each month, October through May, College Club, Seattle.

X-ray Study Club of San Francisco
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly, third Thursday evening.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Medical Members' meeting held monthly on third Friday at 2:30 P.M. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
Secretary, Dr. J. W. McKay, 1620 Cedar Ave., Montreal.

Société Canadienne-Francaise d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedad Peruana de Radiologia
Secretary, Dr. Victor Giannoni, Apartado, 2306, Lima, Peru. Meetings held monthly except during January, February and March, at the Asociación Médica Peruana "Daniel A. Carrión, Villalta, 218, Lima.

Continental Europe

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. Babaiantz, Geneva.
Secretary for German language, Dr. Max Hopf, Effingerstrasse 49, Bern. Meets annually in different cities.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad: USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

AMERICAN RADIUM SOCIETY

The Twenty-eighth Annual Meeting of the American Radium Society will be held in San Francisco, California, June 28–29, 1946. The details concerning the meeting and the program will be published in the May issue of the JOURNAL.

IVe CONGRÈS DES MÉDECINS ELECTRO-RADIOLOGISTES DE LANGUE FRANÇAISE

Under the presidency of Monsieur de Docteur Delherm, the IVe Congrès des Médecins Electro-Radiologistes de Langue Française will hold its meeting in Paris, France, at the same time as the Congrès de Chirurgie, October 9–12, 1946. The following papers will be presented: "Critical Study of Chronic Rheumatism of the Vertebrae" by Docteur Lachapele; "Contact Radiotherapy" by MM. Cottenot, Lamarque and Gros; "Possibilities and Limitations of Electro-encephalography" by Professeur Baudoin and M. Fishgold. Correspondence in regard to the meeting may be addressed to Docteur Chérigié, 9 rue Daru, Paris VIIIe, France.

PENNSYLVANIA RADIOLOGICAL SOCIETY

The next annual meeting of the Pennsylvania Radiological Society will be held at the Berkshire Hotel, Reading, Pennsylvania, on May 17 and 18, 1946.

MAJOR FRIEDMAN HONORED

Major Milton Friedman, M.C., was presented the Legion of Merit by the Surgeon General, Major General Norman T. Kirk, at the regular monthly meeting of the officers of the Medical Department, on March 21, 1946, at the Army Medical Center, Washington, D. C.

The citation which accompanied the Legion of Merit stated that Major Friedman, during his service as Chief of the Radiation Therapy Section at Walter Reed General Hospital from May, 1942, to January, 1946, had "invented many new and improved instruments and techniques for the treatment of malignant growths."

The citation commended Major Friedman for "his services rendered with unselfish devotion to the welfare of the sick and wounded," and ended with the statement that his service rendered would be "of lasting benefit to mankind."

ORLEANS PARISH RADIOLOGICAL SOCIETY

On the evening of November 8, 1945, at the Röntgen Celebration Dinner, the radiologists of the New Orleans area formed a local radiological society to be known as The Orleans Parish Radiological Society. Dr. Lucien A. Fortier was elected President and Dr. Joseph V. Schlosser, Secretary. Meetings are to be held on the first Tuesday of each month throughout the year.

AMERICAN BOARD OF RADIOLOGY

The American Board of Radiology will conduct examinations at the Palmer House, Chicago, Illinois, on November 27 to December 1, 1946. This will be the only examination held during 1946. All those wishing to appear before the Board at this time *must* have their application on file by September 1, 1946.

B. R. KIRKLIN, *Secretary*
American Board of Radiology
Mayo Clinic, Rochester, Minn.

CORRECTION

In the article entitled "Roentgenologic Findings in the Lungs of Victims of the Cocoanut Grove Disaster" by Finland, Ritvo, Davidson and Levenson, in the January, 1946, issue of the JOURNAL, on page 1, column 2, line 21, the sentence beginning, "There were only . . . " etc., should read: There were only 2 recoveries in the former category and 3 recoveries among 30 patients with respiratory symptoms of Grade 4 severity.

Vol. 55, No. 4

COMMENTS ON THE PREPARATION AND PRESENTATION OF MEDICAL PAPERS

By ROSS GOLDEN, M.D.
NEW YORK, NEW YORK

THE Program Committee of the American Roentgen Ray Society met at the Netherland Plaza Hotel in Cincinnati on December 2, 1944, to plan for the meeting of the Society in 1945. The importance of proper preparation of the papers and arrangement of material for presentation at the meeting was discussed. Failure to arrange a presentation properly reduces its effectiveness, wastes the time of the listeners and prolongs the sessions beyond the specified time limits. The Chairman, in behalf of the Committee, was requested to outline some suggestions for authors, a copy of which would be sent to each individual who received a place on the program. The intention of the Committee was, in particular, to aid the younger members of the Society. At the request of the Office of Defense Transportation, the 1945 meeting of the American Roentgen Ray Society was cancelled. However, the Editor of the AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY requested that these suggestions be published.

TWO TYPES OF PREPARATION REQUIRED

When a paper is to be presented before a medical society, it is necessary to prepare actually *two* papers, namely:

1. A paper for publication in which the material is arranged in its permanent form as the author wishes it to appear in print.
2. An abbreviated or abstracted version for oral presentation at the meeting.

Medical societies usually require that the completed manuscript, ready for publication, be handed to the Secretary at the time the oral presentation is made. It is advisable to prepare the manuscript for publication first.

PREPARATION OF MEDICAL AND SCIENTIFIC MATERIAL FOR PUBLICATION

Fishbein has published a little book entitled, "Medical Writing" which should be read by every doctor who proposes to write a paper. It contains many excellent suggestions and discusses the problems of preparation of manuscripts much more elaborately than can be done here.

The prime objective of medical writing should be clarity and brevity. To this end, a certain technique in the preparation of a paper is necessary.

The material of which the paper is composed must be collected in the form of notes, cards, or perhaps as a mental outline.

The first draft of the paper is then made. Some writers prefer to dictate the first draft to a stenographer. My personal preference is to write it in long hand. With the latter method immediate corrections and rearrangements are more easily made. For experienced writers the dictation technique may be satisfactory but I have the impression that in many instances the result is likely to be more verbose than if the writing is done in long hand, where unnecessary words and phrases are easily seen. The author may prefer to type the first draft himself rather than to write it in long hand. However it may be written, the first draft should be corrected and changes made in the arrangement of sentences, in their sequence in paragraphs, or in the sequence of paragraphs, as indicated.

The second draft may be written by hand or may be typewritten, preferably triple-spaced to permit easy correction of words, the interpolation of words, phrases or sentences, and the rearrangement of sentences and paragraphs. My custom is to make a third draft also triple-spaced. The fourth draft can be written double-spaced, as it must be for presentation to the printer, just as if this were to be the final copy. The manuscript may be laid away for a period of time, for days or weeks, and then read again. Undoubtedly new corrections and

refinements will become obvious. The third or fourth draft should be presented to a friend who is familiar with the subject, for his criticism. This critic should be selected with care. He should have sufficient interest in the author or the subject to read the manuscript carefully and to make criticisms and suggestions freely, without fear of offense. It is useless to present the manuscript to someone who will merely glance through it and say that it is a fine job. A good critic will usually detect statements which seem clear to the writer but which may be interpreted differently by readers.

Division of Paper into Topics or Headings. The subject matter for most papers can be arranged under several main headings or divisions which should be put into the manuscript. As examples may be mentioned: "Introduction," under which the background and purpose of the paper are stated; "Literature," under which previous publications bearing on the subject are reviewed; "Material," under which is described the substance of the paper and which may require additional subdivision; "Discussion," under which the significance of the material is set forth; and "Summary" or "Conclusion," under which the significant points made in the paper are briefly reviewed and which will be discussed further.

Separation of a paper into divisions in this way is helpful in arranging the data and the author's ideas in logical order, and adds greatly to the ease of reading. This device is used by newspaper writers and by magazine writers to break up long columns and make them look less long and forbidding. The scheme given above is simple and will not be adequate for all papers. Additional headings and more elaborate division will often be necessary.

Clarity. Clarity in writing is obviously based on clear thinking and accurate observation. In putting clear thoughts into writing two points are worth emphasizing: (1) the choice of words and (2) the arrangement of sentences.

1. Words should be selected which are as short and simple as possible. Many words have more than one meaning. The significance of a word may be clear from the context. However, of several words which might be applicable, the one which is least susceptible to different interpretations should be selected. A dictionary of synonyms is helpful.

The propriety of the use of nouns as adjectives is disputed. Fishbien said, "It has long been the policy of the American Medical Association Press to avoid excessive use of nouns as adjectives to modify other nouns." He apparently believes, however, that this rule cannot be applied too rigidly. He used the words "case report" and "manuscript editors."

In "The Loom of Language" Bodmer said (p. 113), "Bible English contains examples of adjectives identical both with the dictionary form of nouns . . . and with the dictionary forms of verbs. . . . Since Mayflower times the number of adjective-nouns . . . has increased yearly. Some pedants who have forgotten their *Bible lessons* in *Sunday School* object to [adjective-nouns]." He stated further that the large and growing group of words which can be verbs, nouns or adjectives is especially characteristic of Anglo-American and implied that this is evidence of the vitality of the language.

In some instances a suffix can be added to a noun or the ending modified to change it to the adjective form, e.g., 'hilum" becomes "hilar" or "hilic" when used as an adjective, although I am not offended by the phrase "the hilum lymph nodes." Such changes in the form of words are called "flexions." Bodmer pointed out that the evolution of the English language has resulted in the elimination of many flexions. This process of simplification is continuing.

Some nouns sound euphonious and make the meaning clear when used as adjectives and do not lend themselves to change into adjective forms. Some nouns must be used unchanged, for example, "the lung shadows." It seems obvious that the purposes of good writing are well served by the use of

certain nouns as adjectives and that it is essentially a question of good taste in the choice of the words to be so used.

2. As a general rule, short sentences are clearer than long complicated ones. The usual tendency of the non-professional writer is to frame his thoughts in long, complex sentences with a number of phrases. Often such sentences at best are awkward and difficult to understand, and at worst are unintelligible. It should never be necessary to read a sentence twice to get its meaning.

Bodmer said (p. 157), "Our first impulse in stating a closely-knit argument is always to keep the threads together with conjunctions. In a first draft we are therefore prone to construct cumbersome sentences which are not necessarily objectionable in speech. Effective writing demands a different technique. Without the vitality they get from tone and gesture, long and involved sentences call for excessive attention and are less suitable for rapid reading than a succession of short ones. So we rightly regard the use of the short sentence as a criterion of good style in French or English writing."

Practically always a complex sentence can be broken down into two or more shorter, simple sentences which make the meaning clear. The use of a semicolon will sometimes serve to indicate a relationship between two ideas which would not be as clear if they were put in separate sentences or if the second were attached to the first as a modifying clause.

Brevity. Brevity can be achieved by the elimination of statements which do not bear directly upon the subject and by using the fewest possible words. The first draft is almost always verbose. It is impossible to put thoughts down in writing without using unnecessary words and phrases. With each subsequent revision it becomes clear that words, phrases or even sentences can be eliminated without loss and usually with improvement in the text. An adjective may be made to replace a phrase, or a phrase a sentence, bearing in mind that, in general, multiple short sentences are better than long complicated ones. The importance of brevity is emphasized humorously in this "poem" from the Canadian Public Health Journal (Slack):

If you've got a thought that's happy—
Boil it down.
Make it short and crisp, and snappy—
Boil it down.
When your brain its coin has minted,
Down the page your pen has sprinted,
If you want your effort printed,
Boil it down.
Take out every surplus letter—
Boil it down.
Fewer syllables the better—
Boil it down.
Make your meaning plain—express it,
So we'll know—not merely guess it,
Then, my friend, ere you address it,
Boil it down.
Skim it well—then skim the skimmings—
Boil it down.
When you're sure 'twould be a sin to
Cut another sentence in two,
Send it on, and we'll begin to—
Boil it down.

All doctors who wish to contribute to medical literature should read Fishbein's Chapter XV on "Revision." He quoted opinions of well-known writers, Sir Clifford Albutt, Sir William Osler, Anatole France and others, on the objectives and technique of revision. Irving Cobb once said that every word of a professional writer represented a drop of sweat. Bodmer said (p. 164), "Effective and lucid writing is hard work. A first draft is never perfect and a good writer is essentially a good self-editor." However, accuracy and clarity must not be sacrificed in the attempt to achieve brevity.

The Title. The title of a paper should indicate clearly the nature of its material. This is of prime importance because the information in the title is the basis for the classification of the article in the Quarterly Cumulative and other Indexes.

The Summary. Practically all medical papers require a summary at the end. This summary should give, in as few sentences as possible, the important elements or the gist of the paper and should include the

conclusions, if any, to be drawn from the information presented therein. A mere statement of what is in the paper is worse than useless. For example: "A hundred cases of something were studied. The effect of this disease on the lung shadows is described. The results of X-ray treatment of this condition are discussed." This type of summary gives no information. A useful summary is one which contains the information necessary for an abstract. Because of the large volume of medical literature, most readers, after a glance at the title and the author's name, go to the summary; some will then read the introduction; and very few will want the details given in the body of the paper. The importance of a good summary cannot be overemphasized.

Illustrations. Illustrations play an important rôle in the presentation of radiologic material. They are expensive and should be selected with care. X-ray shadows are often difficult to describe. An illustration should be used because it will give the reader information difficult or impossible to put into words. Two illustrations should not be used if one will make the point just as well.

In this country x-ray films are usually reproduced in the negative, so they will look like the original. The prints should have a glossy surface. On the *back* of the print the author should write his name, the number of the figure the print will represent and the word "top" at the top of the print so that the printer will know how the half-tone reproduction is to be placed on the page. The pencil used for writing on the back of the print should be soft; otherwise the pressure of the lead will make an elevation on the glossy side which will be reproduced on the half-tone.

The print should be "cropped," that is, the exact extent of the surface to be included in the reproduction should be indicated by lines, preferably made with a red-leaded glass pencil. The important part of the illustration should be reproduced as large as possible. Reproduction of the black area around the margins of a film or the entire abdomen when the disease is in the stomach or in the terminal ileum is useless and expensive. The editors of radiologic journals are well qualified to crop reproductions of x-ray films, but some editors of other medical journals are not so qualified. The writer is well advised to crop his own illustrations. If the special soft red pencil is used, the crop lines can be wiped off without injuring the glossy surface.

In many reproductions of x-ray films arrows are necessary to direct the attention of the reader quickly to the important points of the illustration. Small, inconspicuous arrows are more effective than larger arrows which may dominate the scene unpleasantly. Some photo-engravers have an unfortunate penchant for enlarging arrows far beyond the size of those on the original print. It is sometimes necessary to number the arrows for reference in the legend.

Legends. Every illustration should have a legend. A figure number is necessary but is not sufficient alone. The most effective legend, in my opinion, consists of a topic line and a description. The topic line should give the name of the disease illustrated or the main point of the illustration, and is most effective when printed in slightly heavier type than the rest of the legend. Then should come a brief description, pointing out the main things in the reproduction which the writer wants the reader to notice. This is better accomplished by using simple, straightforward sentences rather than the imperative "note this or that."

Many readers, after reading the summary, will look over the illustrations and form an opinion of the paper without reading further.

In some papers a brief clinical history of the patient may make an effective addition to the legend. This device has been used by certain German writers (e.g., Berg) and impressed me as so effective that I have used it routinely rather than putting the

case history in the text, unless it is one of a series of case histories, some of which are not illustrated.

Whether in the legend or in the text, the summary of the clinical record should be given in complete, flowing sentences, narrative style, instead of nouns and adjectives, without verbs. Medical slang should not be used and abbreviations avoided. The article may be read by ners who might well be puzzled by of the abbreviations used in hospital rds. As a rule, negative information uld be omitted. Occasionally it may be portant to include negative information when it is of particular significance, for example, a negative blood test for syphilis.

The Bibliography. Only those articles bearing on the subject under discussion which have been actually read should be included in the bibliography. If the subject has been discussed in medical literature for years, it is often possible to indicate one or two articles for previous references. This technique is used frequently in Kaufmann's "Pathology," e.g. (Smith and Jones for lit.). The inclusion of unimportant references adds unnecessarily to the expense of publication.

The references used in an article should be listed and checked for accuracy. Because no standard method of arrangement has been adopted, the author should use the bibliographic style of the journal in which the article will be published.

Each reference consists of the name of the author, or authors, the title of the article, the name of the journal, the year in which the article was published, the number of the volume and of the first page of the article. The editorial policy of some journals requires the number of the last as well as the first page. The custom has been to place the author's last name first followed by the initials. If the article has more than one author, some editors prefer to arrange the second, and the subsequent names, in the normal way, that is, with the initials first.

Some writers and some journals, unfortunately, omit the title. For many readers this reduces the value of the reference because the title should indicate the character and scope of an article. Its inclusion may enable a reader to get information he might otherwise miss.

The reference to a book is similarly handled. Following the title, the city in which the book was published, the publisher, the page or chapter referred to and the year of publication are given, but the order varies according to the policy of the journal. If more than one page or chapter is referred to, the numbers should be given in the text.

THE ABBREVIATED VERSION FOR ORAL PRESENTATION

The manuscript as prepared for publication is almost always too long to be read in its entirety at the meeting. Most societies limit the time for each presentation to 15 or 20 minutes. This time cannot be exceeded without interfering with discussion and with other activities at the meeting, or without arousing the resentment of the following speakers or of the audience. Furthermore, the ability of listeners to absorb and retain information is limited. Much detail is worse than useless and only high points should be presented. Therefore, an abbreviated version of the paper should be prepared. This can be done by arranging selected sentences or paragraphs from the original paper or by summarizing paragraphs. The following suggestions seem pertinent.

1. The purpose of the paper should be briefly and clearly stated.

2. An extensive review of the literature is unnecessary and will not be remembered by the listeners. Only those references should be mentioned which are necessary to give a background or to point up the facts to be presented.

3. The material should be arranged compactly to avoid useless repetition. However, repetition of the main point or

points of the paper is sometimes desirable and adds to the effectiveness of the presentation.

4. The use of charts or tables on lantern slides is often effective. They should be made with the letters photographed large enough so that when projected, the audience can read them. Occasionally, speakers use slides which are made in the negative, that is, with the background black and the letters white. This is difficult to read because each letter seems to be a source of ill-defined light. Slides made in the positive, with black letters on a white background, are much better.

5. Lantern slides showing outlines of the material or giving key sentences are useful because with them material is presented through both visual and auditory senses, which is more effective than through either one alone. Such slides often assist the speaker in making the presentation brief and to the point.

6. The number of lantern slides which can be shown is limited by the time allotted for the presentation. An average of more than one slide per minute of allotted time can rarely be used. For example, not more than 15 slides can be shown within a time limit of 15 minutes. If some time is necessary for speaking before or after the slides are shown, or if the slides are of such a character that they require considerable discussion, the number should be reduced.

7. Case histories given orally should be as brief as possible. Negative findings should not be mentioned except in rare instances where the absence of a positive result of a test is of significance. It is unnecessary to say, "The family history was non-contributory." Only positive points with a direct bearing on the problem need be mentioned.

8. At the conclusion of a presentation before an audience, a summary of the points made may or may not be necessary. After some types of presentation, a brief succinct statement of conclusions is advisable.

9. Rehearsal of a presentation is valuable. It familiarizes the speaker with the appearance of his lantern slides when they are projected. It shows him whether or not his material has been arranged so that it can be presented within the time limit.

Discussion of Papers. The discussion of papers at medical meetings is usually limited to five minutes or less. The discussor must resist the temptation to make the discussion into a second paper, no matter how much his interest in the subject has been aroused. Only the point or points should be mentioned which the discussor believes should be emphasized or on which he disagrees with the speaker. Unfortunately, our programs have been so full that discussion has had to be strictly curtailed.

In discussion, it is rarely advisable to show lantern slides or to describe a case in detail. Questions are always in order which will lead the speaker to elaborate briefly on some point which he did not make clear, or which serve to point out a weak spot in the presentation.

Audibility of the Speaker. The sessions of most national medical organizations are held in large rooms where a Public Address System is available for amplification of the speaker's voice. The microphone is usually on a stand located on or near the speaker's desk. Usually the system is adjusted so that the best results are obtained when the speaker's mouth is 12 to 18 inches from the instrument. Placing the mouth too close results in a roaring reverberation which is unpleasant. Unfortunately, when the speaker turns away from the desk to point to something projected on the screen he is usually too far from the microphone. If a second microphone has been provided near the screen he should step over to it. The lapel microphone is better because it stays attached to the speaker. Still better results are obtained when the microphone is suspended from a strap placed around the speaker's neck and rests against his chest six to eight inches from his mouth. He can move freely and turn his head without

modifying the amplification of his voice.

In a room not provided with amplification, the speaker should raise his voice as if addressing the listener farthest from the speaker's platform. The voice should not be lowered. Enunciation of words is improved by taking care to sound all final consonants.

"*Audience Enemies.*" In an interesting discussion of the reading of scientific papers DuBois lists the following as "audience enemies":

1. The Mumbler, who drops his voice to emphasize important points or else talks to the lantern screen instead of to the audience.
2. The Slide Crowder, who packs his slides with typewritten data and shows too many slides.
3. The Time Ignorer, who talks beyond the limit specified in the program or justified by common courtesy.
4. The Sloppy Arranger, who jumbles his material.
5. The Lean Producer, who has poor material.
6. The Grasping Discussor, who, when he gets talking, stays talking.

It is not clear whether Dr. DuBois objected to showing slides with typewritten data on them, or whether it was merely the improper preparation and arrangement of such slides which justifiably aroused his ire. As stated above, I believe that slides with typewritten data on them can be used with great effectiveness if they are properly prepared. To make the lettering clearly visible only the upper case (capitals) should be used. With a fresh ribbon in the typewriter, a piece of carbon paper should be placed against the back of the sheet so that the letter is printed on both sides of the paper, thus increasing the blackness of the letters when photographed even with reflected light. The sentences can be spaced and made sufficiently short so that they can be photographed large enough to make a legible projection. Printing on paper with india ink makes an effective lantern slide.

Objections have been raised to giving an oral presentation from manuscript rather than from memory. Many doctors do not have sufficient training or practice in speaking to make an address of 15 or 20 minutes without reference to extensive notes or to a manuscript. Included in that group, I much prefer to prepare the oral presentation in manuscript form or as an elaborate outline. Without it, I may omit something I intended to say, may add something I did not intend to say, or may not phrase the sentences as clearly as is possible with written revisions. To use a manuscript or an outline in this way, it is not necessary for the speaker to keep his nose buried in the paper. The important point is that the material should be prepared for this particular purpose.

COMMENT

Medical writing has been criticized because it is not "good writing," because it is not "literature" or because it is not enlivened by "humor." The purpose of medical or scientific writing is not to entertain or amuse the reader, nor to produce a piece of immortal "literature." Its purpose is to place on record, accurately, clearly and briefly, information which will be useful. Medical writing should be judged solely as to how well it fulfills this function. Its faults are likely to be verbosity, lack of clarity which may amount to ambiguity, and failure to add worthwhile information to the medical literature. Attainment of the objectives of good medical writing is the result of hard work, conscientious care and experience. Perfection in writing, as in the playing of a musical instrument, is unattainable, but is a distant goal toward which we constantly strive.

SUMMARY

At the request of the Program Committee of the American Roentgen Ray

Society some suggestions for and observations on the preparation and presentation of medical papers have been prepared. A manuscript suitable for publication is usually too long to be read before the Society. An abbreviated version should, therefore, be prepared for oral presentation within the time allotted to the speaker. Both require careful thought, with at least four or five revisions, and with criticism by another person. The objectives of both are accuracy, clarity and brevity. A summary giving briefly the important points of the paper is of prime importance. An explanatory legend for each illustration is essential. In the spoken presentation details should be eliminated and only points of major importance should be included. The number of lantern slides used should be carefully limited. With or without voice amplification, the speaker should take care that he can be heard by every listener in the room.

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BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

Consolidated Indices. Volume II. Author and Subject: 1938–1942, of the American Journal of Roentgenology and Radium Therapy. Cloth. Price, $5.00. Pp. 178. Springfield, Illinois: Charles C Thomas, 1945.

Volume II of the Consolidated Indices, like Volume I, is a work of art. Radiologists again are indeed fortunate in having obtained the services of Dr. George H. Smith for the preparation of this volume. With his experience, skill and scholarship, Dr. Smith has in an admirable manner prepared an Author Index and Subject Index covering all of the original papers, editorials and abstracts published in the American Journal of Roentgenology and Radium Therapy for the years 1938 to 1942 inclusive.

In reviewing Volume II of the Consolidated Indices, I have tried to determine if there were any suggeststions for improvement. I have none to suggest.

Volumes I and II of the Consolidated Indices are "must" books for every radiologist and every library. The reviewer is enthusiastic enough to recommend it to every doctor in clinical and research medicine. The Indices supply a definite need and will be welcomed by all who have occasion to read or consult the American Journal of Roentgenology and Radium Therapy.

A review of this volume would not be complete without complimenting the publisher. The format, the paper, and the print in every way meet the high standard which Mr. Thomas has set for his publications.

Eugene P. Pendergrass

The Osseous System. A Handbook of Roentgen Diagnosis. By Vincent W. Archer, M.D., Professor of Roentgenology, University of Virginia Department of Medicine. Cloth. Price, $5.50. Pp. 320, with 148 plates. Chicago: Year Book Publishers, Inc., 1945.

This is the fourth of a series of diagnostic roentgen handbooks. The author states in his preface that his purpose is to provide a primer for the occasional roentgenographer to help bridge the gap that exists between him and the thoroughly trained roentgenologist.

Basic principles of technique are stressed and general principles of interpretation outlined. The differential diagnosis of fractures in general is discussed and then the subject of fractures and dislocations of the various bones and joints is treated in detail. Under the discussion of fractures and dislocations of each individual anatomic area is included a paragraph on normal non-traumatic simulants which should be of great aid to the relatively uninitiated. These simulants include sesamoids, epiphyseal lines and anatomic variants.

Approximately one-third of the book is devoted to traumatic conditions which carries out Dr. Archer's promise to aid the occasional roentgenographer for it is with such conditions that he will be primarily concerned.

One section of the book deals with the spine, considering fractures, anomalies and diseases in that order. The last two sections are on bone diseases and abnormalities in childhood and adult life respectively.

The illustrations are uniformly good and the text is clear and concise. In so small a book it is difficult to include a great variety of material and yet the author seems to have missed little of importance. He has carried out well his declared intention of aiding the occasional roentgenographer and in so doing has provided a concise handbook on roentgen diagnosis of the osseous system for all roentgenologists.

R. M. Harvey

Selected Papers from the Royal Cancer Hospital (Free) and the Chester Beatty Research Institute. Volume II. 1939–1940. Cardboard. Price, 16/. Pp. 413, with many illustrations. Royal Cancer Hospital (Free), Fulham Road, London, S.W.3, England.

Selected Papers from the Royal Cancer Hospital (Free) and the Chester Beatty Research Institute. Volume III. 1941–1942. Cardboard. Price, 16/. Pp. 345, with many illustrations. Royal Cancer Hospital (Free), Fulham Road, London, S.W. 3, England.

The papers included in these two volumes

have been reprinted from a great variety of publications, mostly British but some Italian and some American. The second volume includes two papers by C. A. Joll, one on the relation of cancer to trauma and the other on cancer of the stomach, both from a general as well as from a surgical point of view. Both these papers are worth careful reading. A third paper by A. L. Abel deals with his experiences in cancer of the rectum. Then comes an important group of articles, some by W. V. Mayneord alone, some by S. B. Adams, and others by J. Honeyburne, L. F. Lamerton, D. W. Smithers and W. V. Mayneord, by M. Lederman and by D. W. Smithers. Most of these have been reprinted from the *British Journal of Radiology*, and their importance to radiologists cannot be exaggerated, because there is no doubt that Mayneord and his co-workers have done much to improve methods of treatment, both with radium and with roentgen rays. Some of these articles deal with what has been called a three-dimensional scheme of determining the distribution of radiation, and the authors describe not only the methods but the apparatus which has been evolved to apply the method.

The remainder of the second volume contains a large series of articles, most of which are reports of experiments carried out with hydrocarbons for the production of cancer.

The third volume likewise contains three groups of articles reprinted mostly from the *British Journal of Radiology*, but some have been reprinted from other publications, including the *Journal of the Chemical Society*, the *Proceedings of the Royal Society of Biology*, and so forth. The first article in this volume deals with thoracico-abdominal gastrectomy for carcinoma of thoracic stomach, by R. W. Raven, of the Royal Cancer Hospital (Free) and Gordon Hospital. Then comes a group of articles by J. R. Clarkson, L. F. Lamerton and W. V. Mayneord, alone or in combination with Joan Honeyburne or with L. F. Lamerton. This group of articles deals with the measurement, by ionization methods, of real energy absorption from a roentgen-ray beam, of depth doses in fields of irregular shape, with the constitutional effects of radiation with special reference to volume dose, with the measurement of radiation for medical purposes, with the physics of intracavitary radium therapy, and finally with a survey of depth dose data. All of these articles are extremely important for radiologists. Then comes a second group of articles on various kinds of malignant tumors, including mucous and salivary gland tumors, cancer of the penis, cancer of the vagina, teleradium treatment of intrinsic cancer of the larynx, cancer of the skin, the spatial distribution of roentgen rays and total energy absorption, the control and treatment of radiation reactions, and a glycerine-gelatin base for irradiation dermatitis and burns. The final group contains a long series of articles dealing with various carcinogenic agents, including pure hydrocarbons and other chemical compounds, the incidence of mammary cancer in mice of an inbred strain, electrical changes in wounds and inflamed tissues, the condensation of some aromatic ketones with ethyl succinate, the effect of prolonged roentgen irradiation on the Congo red index of rabbits, and others.

These two volumes which, owing to war restrictions, have had to be printed on inferior paper, contain a wealth of information, most of which is of capital importance, not only for radiologists but for anyone who has to deal with malignant tumors. The great influence of the work of Mayneord and his associates in the field of radiologic physics as applied to the treatment of tumors cannot be overemphasized, and many of the articles in these volumes are worthy of careful study.

A. U. Desjardins

Nutrition and Chemical Growth in Childhood. Volume II. Original Data. By Icie G. Macy, Ph.D., Sc.D., Director of the Research Laboratory, Children's Fund of Michigan. With a Foreword by Lawrence Reynolds, M.D., Editor of the American Journal of Roentgenology and Radium Therapy. And a Supplement by Julia O. Holmes, Ph.D. Cloth. Price, $10.00. Pp. 1027 (433–1460), with 706 illustrations. Springfield, Illinois: Charles C Thomas, 1946.

In the dedication of this volume, the author records an appropriate quotation by a great student of nutrition, Lafayette B. Mendel, as follows: "The science of nutrition is in the midst of a continual evolution of facts and development of truth. For the present, therefore, we should 'get the facts.'" What sound advice this is when a study is contemplated in a field, be it medicine, science, government, politics, or an investigation into any subject. So often premature conclusions, based on incomplete information, cloud the truth and are, therefore,

worse than useless as they are not only premature but often grossly misleading.

In this volume of 1,027 pages, Dr. Macy and her associates have published information obtained by ten years of careful, detailed and sustained attention directed toward accumulating the facts concerning the growth and development of normal children between the ages of four and twelve years. The information contained in this volume impresses the reviewer as a model of completeness and accuracy. As the author states, the chief purpose of the study is to record data obtained about the growth and development of a few healthy children under conditions similar to those of a normal home environment. In a previous volume by the same author, observations were made of the exact conditions under which the studies were conducted, the method by which the determinations were made, and the data analyzed. In the course of the investigation, over 6,000 five day balances were determined and over 18,000 analytical balances were made of dietary intake, feces and urinary output. A third volume is contemplated which has to do with the interpretation of these results. In part, therefore, Volume II is a continuation of the studies reported in Volume I.

An idea as to the completeness and thoroughness of the study of each of the ten children may be gained from the knowledge that the findings for each subject are recorded in about 100 pages. The material deals in part with the height and weight, skeletal maturation, anthropometric measurements, food intake, observations on the cellular content of the circulating blood, basal metabolism determinations, nitrogen studies on the urine and feces, studies on the teeth, roentgengograms of the bones and gastrointestinal tract, the mineral balance of the body, and various other aspects of the metabolism of normal children of these ages. In addition, there is a supplement of 118 pages which records observations concerning the mineral metabolism of twelve preschool children, collected by Julia Outhouse Holmes.

The reviewer cannot refrain from expressing congratulations to Dr. Macy and her sponsors, the Children's Fund of Michigan, for contributing such a comprehensive, scholarly, and useful compilation of data bearing on these aspects of the development of normal children. On the part of the director of this study, it undoubtedly has taken persistence, determination, a meticulous devotion to details, and a belief in the absolute necessity for the accumulation of such data. For those who are participating in scientific investigations of any type, the guiding principle inferred by her investigations might well be kept constantly in mind, namely, not a single conclusion concerning a disease process is justifiable until it is established clearly that it varies significantly from the normal state.

Cyrus C. Sturgis

The History of Surgical Anesthesia. By Thomas E. Keys. With an Introductory Essay by Chauncey D. Leake, and a Concluding Chapter, The Future of Anaesthesia by Noel A. Gillespie. Cloth. Price, $6.00. Pp. 191, with 34 figures. New York: Schuman's, 1945.

The conquest of pain has been one of the most dramatic events in the history of human progress. Its story has been frequently related by scientists and by lay writers, and it presents a combination of human interest, scientific progress and an understandable personal appeal that makes it an ever popular theme. Anesthesia was acclaimed and accepted as a complete fact for many years and little advance was made on the original observations of Morton, Wells and Crawford Long. It is only in recent years that anesthesiology has become one of the definitive medical specialities and in the last medical generation has arisen an appreciation of the potentialities of research and study in this field. We owe much to the small group of physiologists, pharmacologists and anesthesiologists who have in recent times advanced and widened knowledge of pain and developed new chemicals and methods to control it.

This book gives a satisfying account of the early use of anesthetics but, more importantly, presents an accurate recital of the extremely important advances of this specialty in its newer and wider phase. This is presented with an authoritative personal touch since the author and his collaborators have taken part in the new advances, or know personally, those who have made anesthesiology a major medical and surgical specialty. The modern and definitive synthesis of anesthesia is given in a way worthy of the important development of the subject. The illustrations are well chosen and adequate. Extensive references are given for the text. A complete chronological table gives the events relating to anesthesiology and

its allied subjects; this is followed by a list of sources of the facts thus presented. Selected references for a history of anesthesia are given by subject and also in an alphabetical arrangement.

The introductory essay by Chauncey D. Leake is an invaluable document giving as it does a picture of a science as it develops through the relations of men, and events. In the appendix are given the Morton and Warren tracts on ether with explanatory comment by John Fulton.

The book is an attractive and authoritative history of a method that has become a science. As such it can be read with interest by all. Better still it gives a picture of the maturing of the science that conveys the sense of having been written or approved by those who were importantly concerned in this process. Any one interested in anesthesia, surgery or the historical phases of medicine should own the book. The author and publisher are to be congratulated on their vision and its fruition.

Frederick A. Coller

BOOKS RECEIVED

Consolidated Indices. Volume II. Author and Subject: 1938–1942, of the American Journal of Roentgenology and Radium Therapy. Cloth. Price, $5.00. Pp. 178. Springfield, Illinois: Charles C Thomas, 1945.

The Osseous System. A Handbook of Roentgen Diagnosis. By Vincent W. Archer, M.D., Professor of Roentgenology, University of Virginia Department of Medicine. Cloth. Price, $5.50. Pp. 320, with 148 plates. Chicago: Year Book Publishers, Inc., 1945.

Roentgen Diagnosis of Diseases of the Gastrointestinal Tract. By John T. Farrell, Jr., M.D., Clinical Professor of Radiology, Graduate School of Medicine, University of Pennsylvania; Radiologist, The Lankenau Hospital, Children's Hospital of the Mary J. Drexel Home; Roentgenologist, White Haven Sanatorium; Consulting Roentgenologist, Frederick Douglas Memorial Hospital, Mercy Hospital. Cloth. Price, $5.50. Pp. 271, with 190 illustrations. Springfield, Illinois: Charles C Thomas, 1946.

Clinical Roentgenology of the Heart. Annals of Roentgenology. Volume XVIII. By John B. Schwedel, M.D., Associate Attending Physician, Medical Division, Adjunct Attending Physician, Dept. of Roentgenology, Montefiore Hospital, New York; Attending Electrocardiographer and Associate Visiting Physician in Medicine, Gouverneur Hospital, New York; Lieutenant Commander, M.C.(V).S., U.S.N.R. Cloth. Price, $12.00. Pp. 380, with 749 illustrations. New York: Paul B. Hoeber, Inc., 1946.

The Intervertebral Disc. With Special Reference to Rupture of the Annulus Fibrosus with Herniation of the Nucleus Pulposus. Second Edition. By F. Keith Bradford, M.D., Houston, Texas, and R. Glenn Spurling, M.D., Louisville, Kentucky. Cloth. Price, $4.00. Pp. 192, with 70 illustrations. Springfield, Illinois: Charles C Thomas, 1945.

The 1945 Year Book of Radiology. Diagnosis. Edited by Charles A. Waters, M. D. Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital; Associate Editor, Whitmer B. Firor, M.D., Assistant in Roentgenology, John Hopkins University; Assistant in Roentgenology, Johns Hopkins Hospital. Therapeutics. Edited by Ira I. Kaplan, B.Sc., M.D., Director, Radiation Therapy Department, Bellevue Hospital, New York City; Clinical Professor of Surgery, New York University Medical College. Cloth. Price, $5.00. Pp. 464, with 342 illustrations. Chicago: Year Book Publishers, Inc., 1945.

Selected Papers from the Royal Cancer Hospital (Free) and the Chester Beatty Research Institute. Volume II. 1939–1940. Cardboard. Price, 16/. Pp. 413, with many illustrations. Royal Cancer Hospital (Free), Fulham Road, London, S.W. 3, England.

Selected Papers from the Royal Cancer Hospital (Free) and the Chester Beatty Research Institute. Volume III. 1941–1942. Cardboard. Price, 16/. Pp. 345, with many illustrations. Royal Cancer Hospital (Free), Fulham Road, London, S.W. 3, England.

Classic Descriptions of Disease. By Ralph H. Major, M.D., Professor of Medicine, University of Kansas School of Medicine. Third edition. Cloth. Price, $6.50. Pp. 679, with 158 illustrations. Springfield, Illinois: Charles C Thomas, 1945.

A Textbook of Surgery. By John Homans, M.D., Clinical Professor of Surgery, Emeritus. Sixth edition. Compiled from Lectures

and Other Writings of Members of The Surgical Department of the Harvard Medical School. Cloth. Price, $8.00. Pp. 1278, with 530 illustrations. Springfield, Illinois: Charles C. Thomas, 1945.

The History of Surgical Anesthesia. By Thomas E. Keys. With an Introductory Essay by Chauncey D. Leake, and a Concluding Chapter, The Future of Anaesthesia by Noel A. Gillespie. Cloth. Price, $6.00. Pp. 191, with 43 figures. New York: Schuman's, 1945.

Essentials of Body Mechanics in Health and Disease. By Joel E. Goldthwait, M.D., F.A.C.S., LL.D., Lloyd T. Brown, M.D., F.A.C.S., Loring T. Swaim, M.D., John G. Kuhns, M.D., F.A.C.S. With a Chapter on the Heart and Circulation as Related to Body Mechanics by William J. Kerr, M.D., F.A.C.P. Fourth edition. Cloth. Price, $5.00. Pp. 337, with 128 illustrations. Philadelphia: J. B. Lippincott Company, 1945.

Physical Chemistry of Cells and Tissues. by Rudolf Hober, University of Pennsylvania School of Medicine, Philadelphia, Pa. With the collaboration of David I. Hitchcock, Yale University School of Medicine, Laboratory of Physiology, New Haven, Conn.; J. B. Bateman, Mayo Clinic, Rochester, Minn.; David R. Goddard, University of Rochester, Biological Laboratories, Rochester, N. Y.; Wallace O. Fenn, University of Rochester, School of Medicine and Dentistry, Rochester, N. Y. Cloth. Price, $9.00. Pp. 676, with 70 illustrations. Philadelphia: The Blakiston Company, 1945.

Men Without Guns. Text by DeWitt Mackenzie, War Analyst of The Associated Press. Descriptive Captions by Major Clarence Worden, Medical Department of the United States Army. Foreword by Major General Norman T. Kirk, Surgeon General of the United States Army. Cloth. Price, $5.00. Pp. 47. Illustrated with 137 plates from the Abbott Collection of paintings owned by the United States Government (118 in color). Philadelphia: The Blakiston Company, 1945.

A Bibliography of Visual Literature 1939–1944. Compiled by John F. Fulton, Phebe M. Hoff, and Henrietta T. Perkins. Prepared by the Committee on Aviation Medicine, Division of Medical Sciences, National Research Council, acting for the Committee on Medical Research, Office of Scientific Research and Development, Washington, D. C. Cloth. Price, $3.00. Pp. 117. Springfield, Illinois: Charles C Thomas, 1945.

Uranium and Atomic Power. By Jack De Ment, Research Chemist, The Mineralogist Laboratories; Co-author, Fluorescent Light and Its Applications, etc., and H. C. Dake, Editor, The Mineralogist Magazine; Co-author, Fluorescent Light and Its Applications, etc. Cloth. Price, $4.00. Pp. 343, with illustrations. Brooklyn: Chemical Publishing Co., Inc., 1945.

Abridged Scientific Publications from the Kodak Research Laboratories. Volume XXVI, 1944. Paper. Pp. 292, with illustrations. Eastman Kodak Company, Rochester, New York, 1945.

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., B.S., M.A., 103 Rutledge Ave. Charleston, S. C.

A SIMPLIFIED METHOD FOR MAKING ORTHODIAGRAMS

By J. SHERIDAN BELL, M.D.
NEW YORK, NEW YORK

A SIMPLIFIED method for making orthodiagrams which has been in use for about six years is herewith described. More than six hundred orthodiagrams have been made by this method.

To a sheet of aluminum 39 cm. long, 28 cm. wide, and 0.5 cm. thick four aluminum rods are attached by screws, the apparatus being essentially a table. Two of the rods are curved and partially covered with rubber tubing and placed 14 cm. apart. The rods are 0.8 cm. in diameter and 30 cm. in length; that is, the height of the table is about 30 cm. Rubber tips cover the ends of the straight rods.

In making an orthodiagram, a sheet of paper is placed on top of the table and fastened by two clips. The table is placed over the patient's chest with the curved rods astride the patient's neck and held firmly against the panel behind. The fluorescent screen is placed at a convenient distance from the table. A small lead shot is fastened by adhesive plaster to the back of the screen on the central ray of the

Fig. 1

Fig. 2

roentgen-ray beam, the central ray being located by closing the shutters to a small aperture. The screen and the roentgen tube move together. The gloved hand—the glove is not shown in the photograph—holding a lead pencil with a metal tip is placed between the screen and the table. The observer follows the cardiovascular border from point to point. When a point is marked, the point on the cardiovascular border, the shadow of the extreme tip of the pencil and the shadow of the shot are superimposed. The orthodiagram is completed in the usual manner.*

121 East 60th St.,
New York 22, N. Y.

* Since the question of the amount of radiation received by the examiner might arise, radiation measurements were made on the vertical fluoroscope by Mr. C. B. Braestrup. The conclusions reached from the measurements indicate that when the lead rubber gloves are used, the hand can be in the direct beam for at least sixteen minutes a day without exceeding the maximum permissible daily dose (tolerance dose) of 0.1 roentgen. Since the hand is in the direct beam of roentgen rays for only a few seconds during the making of an orthodiagram, it is obvious from the report submitted that the method is safe.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

NERVOUS SYSTEM

Scott, Wendell G., and Furlow, Leonard T. Myelography with pantopaque and a new technic for its removal. *Radiology*, Sept., 1944, *43*, 241–249.

The authors have found pantopaque a satisfactory contrast medium for myelography. The 3 cc. ampule in which it comes is a sufficient amount for one examination. Its advantage over lipiodol is that it is much more easily removed from the spinal canal. In removing it they do not use a syringe with positive suction but increase intraspinal pressure by having the patient carry out Valsalva's maneuver of taking a deep breath and bearing down as if he were attempting to move his bowels. During the time of increased intraspinal pressure the spinal fluid which is thin and not viscous is displaced, leaving the oil in intimate contact with the needle so that it can be expelled. It comes bubbling out of the needle in droplets, usually mixed with spinal fluid. The Valsalva maneuver is repeated as often as is necessary to remove all the fluid. As a rule, this can be accomplished in twenty minutes but it occasionally requires as long as forty minutes.

The question has been raised as to whether contrast myelography is necessary at all. The authors discuss its use particularly in intraspinal protrusion of the lumbar discs and think that about 60 per cent of the cases can be diagnosed clinically. But for the others, contrast myelography should be used just as contrast roentgenography is used in other parts of the body, as in ventriculography, bronchography, pyelography, cholecystography, etc. It is also indicated in the examination of patients who have persistent or recurrent pain after operation for protruded discs. It is valuable in determining medicolegal responsibility in industrial cases and in the Armed Services. It is also helpful in the identification of multiple protruded discs.—*Audrey G. Morgan.*

Osgood, Ellis C., Arnett, John H., and Lewy, Frederick H. Calcified spinal meningioma. *Radiology*, July, 1944, *43*, 62–64.

Meningiomas of the spinal canal that are sufficiently calcified to cause a roentgen shadow are very rare. In a series of 130 cases of spinal meningioma only 4 per cent showed such calcification.

The authors describe a case in a white woman eighty-four years of age who began to complain of numbness in both hands in June, 1939; this was soon accompanied by pain and weakness, and tactile sensation in the hands was decreased but not lost. A roentgenogram June 19, 1939, showed diffuse demineralization of the cervical and upper thoracic spine. In the canal from the level of the lamina of the 7th cervical vertebra to that of the 2d thoracic there was an almond-shaped area of calcification which almost filled the canal. Roentgen treatment was begun but the patient died in the course of it of cardiovascular complications.

Meningiomas do not show any specific symptoms or clinical signs. The nearest clinical diagnosis that can be made is that of an extramedullary, intraspinal tumor. There is no reason to suspect a specific diagnosis of meningioma unless the roentgenogram shows calcification. If the calcification is confined to the spinal canal the diagnosis of meningioma is probable. In most other calcified lesions in this vicinity the calcification extends outside the canal and invades surrounding structures. The meningioma in this case was of the psammomatous variety.—*Audrey G. Morgan.*

Steinhausen, Theodore B., Dungan, Clarence E., Furst, Joseph B., Plati, John T., Smith, S. Willard, Darling, A. Perry, and Wolcott, E. Clinton, Jr., Warren, Stafford L., and Strain, William H. Iodinated organic compounds as contrast media for radiographic diagnoses. III. Experimental and clinical myelography with ethyl iodophenylundecylate (pantopaque). *Radiology*, Sept., 1944, *43*, 230–235.

The authors discuss ethyl iodophenylundecylate, one of a number of iodinated organic compounds which have been tested as contrast

media for myelography. A provisional chemical formula is given. It was tested on dogs to prove its safety. As compared with iodized poppy-seed oil it is more fluid and more easily injected and removed. It is also absorbed with relative rapidity from the subarachnoid space. Up to 90 per cent of the medium can be removed easily by the method of Kubik and Hampton. Three cases in which it was used are described and photomicrographs given showing the reactions to its use. Pantopaque is a registered trademark for this compound.

In the discussion Capt. Frank Mayfield said he had been using pantopaque since 1942 and found it moves much more rapidly in the spinal canal than lipiodol because it is less viscid. Because of its lower surface tension it fills the root sleeves better and does not show false filling defects. It is easily removed and almost all of it can be recovered by simple aspiration. It is absorbed much more rapidly than lipiodol. Lipiodol is slightly more satisfactory than pantopaque in examining lesions of the cervical area because the pantopaque moves so rapidly that these lesions are sometimes missed.—*Audrey G. Morgan.*

Ramsey, George H., French, J. Douglas, and Strain, William H. Iodinated organic compounds as contrast media for radiographic diagnoses. IV. Pantopaque myelography. *Radiology*, Sept., 1944, *43*, 236–240.

Since the introduction in 1941 of pantopaque as a contrast medium in myelography 150 examinations have been made with it at the Strong Memorial and Municipal Hospitals in Rochester, New York. The technique of lumbar myelography with pantopaque is described in detail and illustrated with myelograms. Pantopaque is particularly satisfactory in myelography of the lumbar region.

An analysis of the results in these cases shows that the findings on pantopaque myelography were accurate in 95 per cent of the cases. The after-care of the patient should be the same as that after routine lumbar puncture. Pantopaque should not be injected in cases in which lumbar puncture is contraindicated nor within ten days of a previous lumbar puncture; injection after a shorter interval may cause subdural and extra-arachnoid extravasations.

Pantopaque was developed in an effort to produce an absorbable medium but its fluidity has proved of as great value as its readier absorbability. Its fluidity makes it possible to carry out myelography rapidly and with very accurate results. It is absorbed probably at the rate of about 1 cc. per year.—*Audrey G. Morgan.*

SKELETAL SYSTEM

Salmon, D. D. Hereditary cleidocranial dysostosis. *Radiology*, April, 1944, *42*, 391–395.

A case of this familial anomaly is described in a soldier of French-Irish descent twenty-one years of age. He had suffered from severe headaches all his life and on entering the Army had felt extreme fatigue and a feeling of weight in the neck and shoulders after calisthenics. He had prominent frontal bosses and a "soft spot" in the midline of the frontal and parietal bones. There had been late eruption of the deciduous teeth and when these were lost late in adolescence some were not replaced by permanent teeth. His shoulders were abnormally mobile and he could bring them together in front. He had had a roentgen examination after an accident in 1940 and had been told of his condition. There was disproportion between the skull bones and bones of the face. The latter were underdeveloped. There was absence of bone tissue in the midline of the frontal bone. The squamous and mastoid port processes of the temporal bone were rudimentary and there was no pneumatization of the mastoid cells. There was poor development of the maxillary sinuses and no development of the frontal sinuses. The fontanelles were not closed and there was defective union of the cranial sutures. There were only small, thin rudiments of the clavicles. In the pelvis there was abnormal separation of the symphysis pubis and blunting of the heads and shortening of the necks of both femurs. The patient's father and sister showed some but not all of these defects.

The cause of cleidocranial dysostosis is not definitely known. It is probably an abnormality of the germ plasm though it may be the absence of certain chemical constituents necessary for the calcification of the membranous bones.—*Audrey G. Morgan.*

Garber, Robert L. Isolated fracture of the first rib produced by muscular traction. *Radiology*, April, 1944, *42*, 395–396.

A case is described in a man of fifty-four, who

tried to lift a large metallic container holding 15 gallons of milk. He suddenly felt a sharp lancinating pain in his right shoulder which compelled him to drop the container and go for medical examination. He was found to have limitation of motion of the shoulder girdle with voluntary splinting of the shoulder. No localized tenderness or crepitation. Roentgen examination showed a complete transverse fracture through the anterior medial portion of the right first rib, presumably at the scalenus tubercle on the upper surface of the rib where the scalenus anticus muscle is attached. There was very slight separation and displacement of the fragments. Uneventful recovery followed in three weeks after simple immobilization.

About 64 cases of isolated rib fracture due to all causes have been reported. Of these 4 cases, about 6 per cent were due to scalenus anticus pull. There was no history of trauma. Most of the patients were laborers or farmers and it is thought the fractures resulted from lifting heavy objects with pull on the scalenus anticus muscle.—*Audrey G. Morgan.*

Ottolenghi, Carlos E. Fracturas de la diáfisis humeral. (Fractures of the diaphysis of the humerus.) *Rev. ortop. y traumatol.*, Jan., 1943, *12*, 201–276.

This is a detailed discussion of 172 cases of fracture of the diaphysis of the humerus, profusely illustrated with roentgenograms showing the types of fracture and the methods of treatment. Illustrative cases of some of the types of fracture are given. These fractures may be transverse or oblique, spiroid or comminuted. The patient is anesthetized and the fracture reduced. If operation is not necessary a plaster cast may be applied or an aeroplane apparatus used and transolecranon skeletal traction or traction with adhesive bands applied. The plaster cast is indicated in general in transverse fractures or oblique ones with only slight inclination. After the cast is applied, frontal and profile roentgenograms should be made to be sure that the fragments are in correct position. Roentgen examination should be repeated frequently as secondary displacement is not uncommon. In very oblique and spiroid fractures continuous traction of one of the types mentioned is indicated. They reduce the fracture longitudinally but have little effect on lateral displacements which may be corrected by direct or indirect pressure.

Treatment of fractures of the humerus in children is relatively simple as the muscles are less well developed and there is less muscle traction. The best method of treatment is reduction of the fracture under local or general anesthesia and immobilization in a thoracobrachial plaster cast.

The average time required for consolidation in these cases was fifty-four days. Of the total number of cases 87.29 per cent consolidated in normal time while consolidation was delayed in 12.71 per cent. Of the total number of cases only 4.65 per cent had to be operated on. The indications for operation are somewhat broader in cases complicated by paralysis of the radial nerve than in others but in recent fractures with this complication treatment may also be non-operative. Operation is indicated only when insufficient reduction has been obtained.

Pseudarthrosis is one of the most serious complications of fracture of the diaphysis of the humerus. It occurred in 13 of the author's cases, or 7.55 per cent. No cases of pseudarthrosis were seen in children. The treatment of pseudarthrosis is always operative. In old cases with atrophy and loss of bone substance metal plates are not indicated but bone grafts should be used.

The most serious sequels of fracture of the humerus are rigidity of the shoulder or elbow joints, refracture and vicious consolidation.

The treatment of gunshot fractures is the same as that for other types of fracture. No attempt should be made to remove the projectile unless it is causing symptoms.

The medicolegal aspects of fracture of the humerus are discussed. The amount of compensation granted depends on the degree of disability produced.—*Audrey G. Morgan.*

Staples, O. Sherwin. Osteochondritis of the epiphysis of the terminal phalanx of a finger. *J. Bone & Joint Surg.*, Oct., 1943, *25*, 917–920.

Staples reports the case of a girl, two and a half years old on admission to the hospital for tuberculosis of the lumbar spine, who during her period of hospitalization developed at the age of four years, pain in the right index finger. There was no history of trauma and examination revealed tenderness, redness and swelling confined to the region of the interphalangeal joint with no evidence of joint effusion. The motions of the finger were normal. Roentgeno-

grams of the hand showed a smaller and denser than normal epiphyseal center of the distal phalanx. Roentgenographic studies of the affected finger were repeated at intervals during nineteen months following the onset of the symptoms. The previously abnormal epiphysis assumed a normal appearance. The roentgenograms showed originally flattening of the center but at no time any tendency to fragmentation. Staples felt that any question of tuberculous involvement could be excluded, and that a diagnosis of osteochondritis was warranted.—*R. S. Bromer.*

Ellis, John D. Compression fractures of the vertebral bodies and other changes mistaken for them. *J. Bone & Joint Surg.*, Jan., 1944, *26*, 139–145.

In this paper the author confines his discussion to the problem of diagnosis of compression fractures of the vertebrae which are of a minor type and may be simulated by non-traumatic conditions. Those which result in complete disintegration of a vertebral body present no difficulty in diagnosis.

A fractured vertebral body with arch intact does not simulate any other type of compression. If the posterior surface of the vertebral body in the lateral roentgenogram is taken as a base line, the upper surface will be found to form an angle with it more acute than a right angle, and the lower surface retains its 90 degree relation with the base line, or is less affected than the upper half. Compression of the upper half is greater in the anterior than in the posterior altitude. If the fracture is not great, the posterior altitude is intact. The anteroposterior measurement of the upper surface is greater than that of the lower surface. Commonly there is a displacement of the upper anterior corner, involving the terminal ridge and the underlying spongiosa. In the anteroposterior view of recent fractures, the loss of the anterior altitude is more difficult to recognize.

In distinguishing between old healed compression fractures and healed non-traumatic lesions of the vertebrae, it is found that, in a fracture, the wedge deformity is roughly preserved and still affects the upper half only, or the upper half out of proportion to the lower half of the body. The increased density in the spongiosa may persist for years. The internal structure of the compressed bone seldom resumes the appearance of the lower half.

It is proved that general spondylosis and osteophyte production in the spine do not result from compression fracture of a vertebra.

Wedge-shaped deformities of the vertebrae, developing independent of trauma, may result from changes peculiar to adolescence. Pathological changes in the end plate and marginal ring such as irregular calcification and failure of calcification, and increased density of the upper and lower portions of the vertebral body, lead to final deformity and irregular calcification of the cartilaginous ring. Sometimes there is a persistence of a separate anterior portion of this ring which has been called "Scheuermann's node," and this is easily mistaken for fracture. This node may occur with or without dorsal kyphosis. The etiology of the condition is unknown.

Ellis gives the following criteria of differential diagnosis of these Scheuermann's nodes from vertebral fractures:

1. The localization is important. The nodes are found most frequently in the lower lumbar region, particularly in the upper border of the fifth vertebra. Compression fractures are commonest in the upper lumbar and lower thoracic vertebrae.

2. The zone of separation is often wide and clear, and like the node, has smooth edges; whereas, irregular edges are seen in compression fractures.

3. The node is often larger in size than a marginal fragment should be.

4. The dislocation of the fragment or node is often considerable; it may be somewhat upward and anterior. Dislocation of a marginal fracture is slight and generally downward and anterior, corresponding to the lane of compression of the superior surface of the body of the vertebra. The general contour of the centrum or vertebral body remains normal in a case of persistent node; but in a case of fracture, it varies from slight compression of the upper surface to a wedge-shaped deformity.

5. The mechanogenesis of the persistent node may be abnormal lumbar-extension strain or distraction in childhood, and not a single injury; whereas, a compression fracture is the result of flexion of the spine, a shearing force, and an impression of force on the disc and the upper surface of the centrum, leaving its typical mark.

In the first year of life, the vertebral body, in

the lateral roentgenogram, appears a rectangle with blunted corners; both the anterior and posterior borders of the terminal plates present a notching. This space is ringlike in form, extending entirely around the vertebral margin. The stepped space is lower toward the front than at the side or back. It is normally filled with cartilage, termed by Schmorl the "Randleiste," or it may be referred to as the "marginal ring."—*R. S. Bromer.*

Lagomarsino, Enrique H., and dal Lago, Héctor. Radiología de las artrodias apofisarias intervertebrales. (Roentgenology of the intervertebral apophyseal processes.) *Rev. ortop. y traumatol.*, April, 1943, *12*, 333–346.

Diagnosis in lumbar or lumbosacral pain is very difficult. It was formerly believed that the diagnosis could be made by roentgen examination in the oblique projection intermediate between the frontal and sagittal planes; if the joint interspace was blocked it indicated arthritis and this diagnosis was strengthened if there was also irregularity in the joint surfaces of the processes and hyperostosis and osteoporosis of the processes. But Putti and Logroscino in 1937 found in a comparative anatomical and roentgenological examination of 75 spinal columns that the joint changes that often occur after thirty years of age are not visible roentgenologically in the beginning stages and often not even in the advanced stages. They found that arthritis of the intervertebral joints does not occur before thirty years of age.

But in the examination of 25 spinal columns in young men twenty-five years of age or less admitted for traumatism the authors found the changes that have been described as characteristic of intervertebral arthritis. They conclude that horizontal, lateral and oblique projections are necessary in examining for this condition. The oblique projection alone is insufficient for diagnosis. They found that the signs mentioned above are not sufficient for diagnosis if single ones are found alone. The probability of arthritis increases if several of them are associated and if they are very marked in degree.

It is very hard to define a normal roentgen image of these joints as there is great anatomical variability between different columns, in different parts of the same column and in the columns of individuals of different ages and constitutions.

In the roentgen examination of 132 cases of lumbago they found syndromes definitely indicative of arthritis in only 2 cases. Therefore they hold that for a definite diagnosis not only must very careful roentgen examination be made in various projections but that the clinical picture must be examined with equal care.—*Audrey G. Morgan.*

Gill, A. Bruce. Relationship of Legg-Perthes disease to the function of the thyroid gland. *J. Bone & Joint Surg.*, Oct., 1943, *25*, 892–901; correction, Jan., 1944, *26*, 228.

In 1936, Cavanaugh, Shelton and Sutherland reported studies in 5 cases of Legg-Perthes' disease and stated that in all of them they found definite evidence of metabolic (thyroid) deficiency. Gill accepts their observation so far as the clinical evidence is concerned, namely, the presence of colloid goiter in mothers, maternal aunts and other members of the family; retarded development of the bones of the hand; other physical stigmata such as delayed and faulty dentition, hypogenitalism, cryptorchidism, enuresis, palpable thyroid gland and dryness of the skin and hair. He doubts, however, that the administration of thyroid extract materially shortened the period of regeneration or healing of the head of the femur.

From a systematic study of 20 cases, which included family and medical histories, physical and mental development of the child, complete physical examination of all parts of the body, orthopedic examinations, roentgenographic studies of the skull and bone age of the hands and of the hips involved, and laboratory examination, he concluded that no evidence was presented that the condition was due to hypothyroidism. He doubted that all types of osteochondritis juvenilis are manifestations of the same pathological process and that they are due to one and the same cause. Difficulties in diagnosis of mild and borderline cases of hypothyroidism should be recognized and particularly so in relation to other endocrine deficiencies.—*R. S. Bromer.*

Oppenheimer, Albert. Arthritis of the acromioclavicular joint. *J. Bone & Joint Surg.*, Oct., 1943, *25*, 867–870.

The clinical syndrome which has come to be

designated as "painful shoulder syndrome" may be produced by different lesions, among which arthritis, bursitis and neuralgia, due to disease of the cervical spine, are perhaps the most common. Oppenheimer believes that arthritis of the acromioclavicular joint seems to induce this syndrome more frequently than the scant references in the literature would lead one to suspect. In his cases, the clinical manifestations were indistinguishable from those produced by arthritis of the shoulder joint, subacromial and subdeltoid bursitis and radicular neuralgia.

In some of his patients, the joint capsule was found to be enlarged, casting an olive-shaped or globular shadow in the roentgenogram. In others there was marginal overgrowth along the articular bones, with roughening of the joint surfaces and widening of the joint space, probably caused by effusion. The subchondral bone had a honeycombed appearance. In still others there was evidence of a definite osteoarthritis of the joint without evidence of other disease of the shoulder joint, muscles or bursae or the cervical spine.

He states that roentgen therapy in very small doses resulted in clinical cure in a series of patients. Other modes of treatment had not been effective.—*R. S. Bromer.*

Moore, John R. Delayed reduction of fractures. *J. Bone & Joint Surg.*, Jan., 1944, *26*, 151–176.

Since February 15, 1935, Moore has used the following method for reduction and handling of fractures:

1. All fractures are examined immediately for nerve and vessel injury, and for such complications as head, spinal cord, and internal injuries, etc. The treatment of these major problems is instituted immediately by the department concerned.

2. All fractures of the long bones are immobilized immediately in plaster of paris splints which routinely include the joint above and the joint below.

3. Roentgenograms are taken at the convenience of the department of radiology, either immediately or the following day.

4. One day a week is set aside for the reduction of fractures.

Following immobilization at the time of admission, the patient is kept under observation in the Accident Dispensary for an hour, and is then allowed to return, or is admitted to the hospital, depending upon the absence or presence of complications, facilities for home care, etc. He is instructed to report on the day set aside for reduction and special emphasis is placed upon pre-anesthesia preparations. On the morning of the reduction, a cylindrical section of plaster, 3 to 4 inches in width, is removed at the site of the fracture in fractures of the long bones. If traction is required to maintain reduction, a single pin is inserted in each major fragment. The temporary splints employed in other types of fractures are removed. These latter fractures are reduced and are subsequently splinted according to the standard methods. Reduction is uniformly successful, provided muscle relaxation is obtained. Generally speaking, the effort required for reduction is greater than that observed in immediate reduction, yet a closed reduction is obtainable in the majority of cases; open reductions are comparatively few. Following reduction, the patient is permitted to go home or is admitted to the hospital depending primarily upon the status prior to reduction.

Moore believes the ideal time for delayed reduction is between the fourth and eleventh day. Compound fractures, simple dislocations, compound dislocations, and fractures complicated by nerve and vessel injury, should be regarded as emergencies. He found that the time required for repair in the group of delayed reductions would seem to date from the time of fracture, rather than from the time of reduction. Union and function appeared to be unhampered.

Moore found that delayed reduction provided the opportunity for excellent teamwork, and the best trained individuals are readily available for all purposes. The patient is adequately prepared for anesthesia. He does not urge delayed reduction. If teams which provide well trained supervision are available for immediate reduction, the latter should be done. In localities where well trained supervision is not at hand, it would appear that delayed reduction is by far the better procedure. He concludes in defense of delayed reduction that "a well-supervised delayed reduction is better than a poorly supervised immediate reduction."

The study is based on a total of 7,009 fractures. The article is well illustrated with roentgenograms of fractures and results obtained.—*R. S. Bromer.*

Clement, Baxter L. March fractures. *J. Bone & Joint Surg.*, Jan., 1944, *26*, 148–150.

Baxter studied a series of 32 cases of march fracture, all confirmed roentgenologically, which were encountered in a Basic Training Center Station Hospital. The patients were undergoing their first few weeks of military training and undoubtedly were being subjected to unusual foot strain in comparison with their civilian life. Their average length of military service was eleven weeks. The symptoms were typical, consisting of localized tenderness directly proximal to the metatarsophalangeal joint of the metatarsal involved, and swelling on the dorsum of the foot. The fracture line was oblique in all early cases. The second and third metatarsals only were involved. The fracture line appeared on the medial surface of the metatarsal in 29 of the 32 cases. The second and third metatarsals were of greater length as compared with the first metatarsal in all but 2 cases. Baxter suggests that, in a foot in which the second and third metatarsals are longer than the others, march fractures may occur from stress and strain as a result of abnormal bony leverage and spasm of the irritated interossei dorsales and lumbricales muscles. The fact that the fracture line was oblique would tend to support this theory, likewise the occurrence of the fracture line on the dorsomedial aspect of the shaft.

If a march fracture is suspected clinically, even though the initial roentgenogram appears negative, Baxter applies a metatarsal pad for the support of the second and third metatarsals and prescribes complete rest. This procedure he believes limits the period of total disability, should a fracture later be identified roentgenographically.—*R. S. Bromer.*

Carlson, Glenn D., and Wertz, Royal F. March fracture, including others than those of the foot. *Radiology*, July, 1944, *43*, 48–54.

Since the beginning of the second World War there has been a decided increase in the incidence of march fracture; it occurs chiefly in fresh recruits who have led sedentary lives and who have to march long distances carrying excessively heavy packs.

It usually occurs in the metatarsals but may occur in other bones. The authors discuss 70 cases seen in the roentgen service of the Brooke General Hospital, Fort Sam Houston, Texas, from January, 1942 to April, 1943. Sixty-six were in the metatarsals, 3 in the femur and 1 in the os calcis. Practically all the cases showed varying degrees of periosteal reaction while only 13 showed definite fracture lines. The age of the patients varied from twenty to forty-five years, the average being twenty-two. Of the 66 men with metatarsal fractures only 5 were placed on limited duty. Of the others, 11 were given treatment in the out-patient clinic consisting chiefly of arch supports and proper fitting of shoes. The other 50 were treated in the hospital with a plaster walking boot for an average of three weeks, followed by ten to fourteen days of physiotherapy, and proper arch supports. The 3 men with fractures of the femur and the 1 with a fracture of the os calcis were placed on limited duty.

The chief point in diagnosis is to differentiate from malignant tumor and so avoid amputation or other unnecessary surgery. If there is a globular bony mass around a bone shaft, a demonstrable fracture line or even a periosteal proliferation with a history of marching there need be no fear of malignancy.—*Audrey G. Morgan.*

Satanowsky, Sara, Perruelo, Nicolás, and Kohn, Alfredo. Tratamiento de fracturas trocantéricas del fémur en personas ancianas por el enyesado de Ducroquet. (Treatment of trochanteric fractures of the femur in old people with Ducroquet's plaster cast.) *Rev. ortop. y traumatol.*, April, 1943, *12*, 309–332.

The authors recommend Ducroquet's plaster cast for the treatment of trochanteric fractures in old people. Twenty cases are described and freely illustrated with photographs and roentgenograms. This cast is applied to both the normal and fractured legs from the toes to the root of the thigh. Two cross-bars are attached to the cast above the ankles and above the knees so that the legs in their casts, the cross-pieces and the pelvis form a rigid trapezium which prevents movement of the fragments. If this method does not altogether prevent scars it greatly decreases their extent and duration. A roentgenogram should be made of course when the cast is applied to see that the fragments are in good position and others periodically during the two and a half months that it is left on to see that no displacement has occurred. The joints on the normal side recover normal movement very quickly after the cast is removed, and those of the injured side naturally

more slowly, which is the case with any sort of treatment.

Four of these patients died, or 20 per cent; the method of treatment had nothing to do with the deaths, however. One died of diabetic coma which set in the day the cast was applied, 2 died in the week following the application of the cast and the other, three weeks after from asystole. With better selection of patients, taking into account the poor general and circulatory condition of these old people, the mortality could doubtless be greatly reduced.

Of the other 16 patients, from sixty to eighty-nine years of age, the fracture consolidated in perfect position in 14, and the other 2 did not return for re-examination after having been discharged in good condition.—*Audrey G. Morgan.*

Chiodin, Leopoldo, and Rabbi, Rodolfo A. Linfogranulomatosis maligna con lesions óseas. (Malignant lymphogranulomatosis with bone lesions.) *Rev. ortop. y traumatol.*, April, 1943, *12*, 347–362.

Malignant lymphogranulomatosis is one of the various names applied to the disease first described by Thomas Hodgkin in 1832 as Hodgkin's disease. Up until about fifteen years ago it was thought that this disease was limited to the lymphatic system but it has recently been found that the bones may also be involved; this involvement has been reported in from 10 to 34 per cent of cases. These bone lesions may be compared to bone metastases in other malignant tumors. They are seen chiefly in adults and the bone lesions generally seem to be secondary to the gland involvement. The bone lesions may be osteolytic or osteoblastic but the former predominate. No pathognomonic roentgen signs have been found which differentiate these bone lesions from other bone metastases. Accurate diagnosis requires clinical study and histopathological examination.

The authors describe a case in a girl of twelve which was unusual from the early age of the patient and the fact that the bone lesions preceded the gland lesions clinically. She was admitted to the hospital with pain in the lumbar region radiating to both lower limbs. Roentgen examination showed bone changes which resembled those of Pott's disease. Cervical, inguinocrural and iliac glands enlarged. Examination of bone and gland material from the crest of the ilium and a superficial inguinal gland showed the typical picture of malignant lymphogranulomatosis. The progress of the disease continued in spite of roentgen treatment and the patient was discharged in a condition of cachexia. Roentgenograms and photomicrographs of the histopathological findings are given.

Roentgen treatment gives at least temporary relief in this disease. Heublein's method of irradiating the whole body with radiation of low intensity is at present very much in favor.—*Audrey G. Morgan.*

Schajowicz, Fritz, and Mondolfo, Silvano. Morfología, histogénesis biología de la célula gigante de los tumores a células gigantes. (Morphology, histogenesis and biology of the giant cell of giant cell tumors.) *Rev. ortop. y. traumatol.*, Jan., 1943, *12*, 277–308.

The authors base their discussion of the giant cell on 24 cases of giant cell tumor recently examined and on previous pathological experience in the hospitals of Vienna and Bologna.

The article is profusely illustrated with photomicrographs of the different stages of development and degeneration of these cells.

Three types of giant cells are described which correspond roughly to different degrees of benignancy or malignancy of the tumors. In very malignant tumors there is a fourth type which is smaller and with fewer nuclei than the other types; the nuclei are generally large and hyperchromatic with one or several large nucleoli, sometimes showing atypical mitosis. But in order to judge the nature of the tumor there must be a decided predominance of one or the other of these types, as there are always variations in the cell types in the same tumor.

There are three theories in regard to the histogenesis of these cells: the osteoclastic, the vascular and the mesenchymal. The authors conclude that these cells originate from a young and immature mesenchyme, either directly or indirectly by way of transformation into an endothelial type. This mesenchymal tissue is capable of differentiation into collagen fibers, osteoid tissue, bone or cartilage, as well as into these tumor cells.

As these cells are really tumor cells they have no physiological function; this explains why they are more abundant than would be required for any physiological need. They are deviations from a normal phagocytic function.

The giant cell may show two types of de-

generation, either pyknosis and karyorrhexis of the nuclei with increased eosinophilia of the protoplasm or karyolysis, generally associated with vacuolar degeneration of the protoplasm. —*Audrey G. Morgan.*

Kleinberg, Samuel. Osteoid osteoma. *Am. J. Surg.*, Dec., 1944, *66*, 396–401.

This is an instructive consideration of osteoid osteoma, otherwise known as non-suppurative or sclerosing osteomyelitis. The author states that the condition may be diagnosed or at least strongly suspected from the presence of three significant features. The first of these is pain which is always in the same location, is of greatest intensity over a small area coincident with the site of involvement and may be surrounded by a large surface with less severe pain. The pain gradually increases in the course of some months from mild and intermittent to severe and constant. The second feature is tenderness to pressure over the region of greatest pain; the only condition under which this sign may not be elicited is when the part is inaccessible to examination. The third feature is the demonstration in roentgenograms of an oval area of rarefaction surrounded by a zone of sclerosis of variable width. The location of the rarefaction is approximately at the site of pain and tenderness.

There is no general systemic disturbance due to the disease and the customary laboratory investigations are negative.

By way of illustration he presents 3 cases, each offering different diagnostic problems. The regions involved were the upper end of the fibula, the right lamina of the second lumbar vertebra and the astragalus, respectively. Each patient was rendered entirely symptom-free by complete surgical removal of the lesion. The paper is illustrated by good reproductions of roentgenograms made of each case.—*Angus K. Wilson.*

Kositchek, Robert J. Monocytic leukemia associated with bone changes. *Ann. Int. Med.*, Dec., 1943, *19*, 1008–1013.

The purpose of this paper is to present a case of monocytic leukemia which demonstrates the bone involvement previously observed in the lymphocytic and myelogenous types of leukemia. A review of the literature has failed to reveal similar bone involvement in leukemias in which the dominant cell is a monocyte or one of its immature forms. The changes noted were softening and absorption in the medullary portion of many of the long bones, increased porosity produced by the widening of the haversian canal, and cystic changes which may be indicative of neoplastic invasion. The bones involved included the skull, the head of both humeri, the right clavicle, the pelvis and the head and neck of both femurs. The patient received considerable relief of his symptoms by roentgen therapy over the painful extremities. —*J. J. McCort.*

Hench, Philip S., and Rosenberg, Edward F. Palindromic rheumatism. *Arch. Int. Med.*, April, 1944, *73*, 293–321.

The authors describe an unusual, often recurring disease of joints and adjacent tissues, 34 cases of which have been studied in the Arthritis Service of the Mayo Clinic since 1928. Its outstanding features are multiple afebrile attacks of acute arthritis and peri-arthritis and sometimes also of para-arthritis with pain, redness, swelling and disability generally of only one but sometimes of more than one small or large joint in an adult of either sex. The attacks appear suddenly and develop rapidly. They generally last only a few hours or days and then disappear completely but they recur repeatedly at short or long irregularly spaced intervals. Despite the frequent recurrences and the transitory presence (in some cases at least) of an acute or subacute inflammatory polymorphonuclear exudate in the articular tissues and cavities, little or no constutional reaction or abnormality is revealed by laboratory tests and no significant functional pathologic or roentgenographic residues occur even after years of disease with scores of attacks.

These patients did not have symptomatic residues despite their repeated attacks and, likewise, roentgenographic residues did not develop in joints. Of the 164 roentgenograms of various joints made in the 34 cases, 150 (91 per cent) revealed nothing significant; the remaining 14 (9 per cent) showed changes regarded as unrelated to the chief complaint. These few evidences of definite articular or osseous change give little support to the idea that the acute, recurrent arthritis, the authors describe, produced significant articular damage reflectable in roentgenograms. Thus since more than 90 per cent of the roentgenograms of these

more slowly, which is the case with any sort of treatment.

Four of these patients died, or 20 per cent; the method of treatment had nothing to do with the deaths, however. One died of diabetic coma which set in the day the cast was applied, 2 died in the week following the application of the cast and the other, three weeks after from asystole. With better selection of patients, taking into account the poor general and circulatory condition of these old people, the mortality could doubtless be greatly reduced.

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This is an instructive consideration of osteoid osteoma, otherwise known as non-suppurative or sclerosing osteomyelitis. The author states that the condition may be diagnosed or at least strongly suspected from the presence of three significant features. The first of these is pain which is always in the same location, is of greatest intensity over a small area coincident with the site of involvement and may be surrounded by a large surface with less severe pain. The pain gradually increases in the course of some months from mild and intermittent to severe and constant. The second feature is tenderness to pressure over the region of greatest pain; the only condition under which this sign may not be elicited is when the part is inaccessible to examination. The third feature is the demonstration in roentgenograms of an oval area of rarefaction surrounded by a zone of sclerosis of variable width. The location of the rarefaction is approximately at the site of pain and tenderness.

There is no general systemic disturbance due to the disease and the customary laboratory investigations are negative.

By way of illustration he presents 3 cases, each offering different diagnostic problems. The regions involved were the upper end of the fibula, the right lamina of the second lumbar vertebra and the astragalus, respectively. Each patient was rendered entirely symptom-free by complete surgical removal of the lesion. The paper is illustrated by good reproductions of roentgenograms made of each case.—*Angus K. Wilson.*

Kositchek, Robert J. Monocytic leukemia associated with bone changes. *Ann. Int. Med.*, Dec., 1943, *19*, 1008–1013.

The purpose of this paper is to present a case of monocytic leukemia which demonstrates the bone involvement previously observed in the lymphocytic and myelogenous types of leukemia. A review of the literature has failed to reveal similar bone involvement in leukemias in which the dominant cell is a monocyte or one of its immature forms. The changes noted were softening and absorption in the medullary portion of many of the long bones, increased porosity produced by the widening of the haversian canal, and cystic changes which may be indicative of neoplastic invasion. The bones involved included the skull, the head of both humeri, the right clavicle, the pelvis and the head and neck of both femurs. The patient received considerable relief of his symptoms by roentgen therapy over the painful extremities. —*J. J. McCort.*

Hench, Philip S., and Rosenberg, Edward F. Palindromic rheumatism. *Arch. Int. Med.*, April, 1944, *73*, 293–321.

The authors describe an unusual, often recurring disease of joints and adjacent tissues, 34 cases of which have been studied in the Arthritis Service of the Mayo Clinic since 1928. Its outstanding features are multiple afebrile attacks of acute arthritis and peri-arthritis and sometimes also of para-arthritis with pain, redness, swelling and disability generally of only one but sometimes of more than one small or large joint in an adult of either sex. The attacks appear suddenly and develop rapidly. They generally last only a few hours or days and then disappear completely but they recur repeatedly at short or long irregularly spaced intervals. Despite the frequent recurrences and the transitory presence (in some cases at least) of an acute or subacute inflammatory polymorphonuclear exudate in the articular tissues and cavities, little or no constutional reaction or abnormality is revealed by laboratory tests and no significant functional pathologic or roentgenographic residues occur even after years of disease with scores of attacks.

These patients did not have symptomatic residues despite their repeated attacks and, likewise, roentgenographic residues did not develop in joints. Of the 164 roentgenograms of various joints made in the 34 cases, 150 (91 per cent) revealed nothing significant; the remaining 14 (9 per cent) showed changes regarded as unrelated to the chief complaint. These few evidences of definite articular or osseous change give little support to the idea that the acute, recurrent arthritis, the authors describe, produced significant articular damage reflectable in roentgenograms. Thus since more than 90 per cent of the roentgenograms of these

patients fail to show abnormalities after a total of many decades of illness and hundreds of attacks it must be concluded that the few articular changes noted were coincidental. When the temporary severity of the clinical symptoms and of the histopathological reaction is considered, it is indeed surprising to find no significant roentgenographic residues.

The chief points which distinguish these cases of palindromic rheumatism from instances of rheumatoid arthritis include the following: (1) the totally different pattern of the arthritis (one of numerous short attacks and persistent functional restitution); (2) the tendency for only one or two joints to be involved in an attack; (3) the frequently isolated short attacks of para-arthritis; (4) the general absence of significant constitutional reaction; (5) the relative absence of effect of season and weather; (6) the sedimentation rate which is relatively normal, or only moderately and transiently elevated; (7) the moderate increase (rather than decrease) in blood fat; (8) the persistently negative roentgenograms; (9) the different pathological reactions. The greatest and most convincing difference is the persistent absence or chronic arthritis even after scores or hundreds of attacks and years of disease.

Palindromic means simply recurring or returning and is so defined in current non-medical and medical dictionaries. The designation palindromic rheumatism has been approved for inclusion in the Standard Nomenclature of Disease and appears with numerical designations in the third edition. The authors believe that it will be useful and satisfactory until a better etiologic term can be applied.—*J. J. McCort.*

Fried, B. M. Chronic pulmonary osteoarthropathy; dyspituitarism as a probable cause. *Arch. Int. Med.*, Nov., 1943, *72*, 565–580.

Four cases of chronic pulmonary osteoarthropathy in patients with bronchiogenic cancer are reported. While the etiological relationship between the pituitary gland and acromegaly is no longer contested, the causative factor of chronic pulmonary osteoarthropathy remains problematic. An analysis by the author of the 4 cases here reported reveals data pointing toward the conception that the megalia cutis et osseum resulted in all probability from a disturbance in the function of the organs of internal secretion. In Case I, the patient had an acromegalic appearance, tufting of the terminal phalanges of the fingers and toes; splenomegaly, atrophy of the testicles and a large adenohypophysis showing pronounced hyperplasia of eosinophilic element. Case II had an acromegalic appearance, "bull-dog" scalp, hirsutism, macroglossia, tufting of the terminal phalanges of the fingers and toes and thickening of the cranial vault. Case III showed mongoloid features, secondary male characteristics, large cortical adenoma of the adrenals, several adenomas of the thyroid and hyperplasia of the cells of the anterior lobe of the pituitary, with eosinophilic cells in the majority. Case IV had coarse acromegalic features, gynecomastia, several adenomas of the adrenals, roentgenologic evidence of enlargement of the sella turcica and tufting of the terminal phalanges of the fingers and toes.

The data obtained from this study are believed by the author to favor the conception that diffuse osteoarthropathy found in neoplastic diseases of the lung is, in all probabiilty, caused not by toxins or by circulatory disturbances, as postulated more than a century ago, but by an endocrine imbalance akin to acromegaly and to pachydermia with pachyperiostosis.—*J. J. McCort.*

Brailsford, James F. Diagnosis and treatment of ostoclastoma. *Radiology*, July, 1944, *43*, 35–38.

Osteoclastoma is also known as myeloid sarcoma, myeloma and giant-cell sarcoma. It usually occurs in the ends of the long bones in young adults. The roentgen picture is typical. The tumor slowly dissolves the bone. It does not infiltrate as sarcoma does and the boundary between tumor and normal tissue is often clearly defined. The bone cortex is gradually dissolved and when it becomes very thin it bulges with the growth of the tumor. At this stage there may be a thin periosteal accretion of new bone. The joint cartilage is usually still intact when the patient comes for treatment. Decalcification may cause spontaneous fracture, which may be the first indication of the tumor.

There are a number of other conditions which resemble this tumor roentgenologically but with sufficient experience and skill the roentgenologist can learn to differentiate them. The chief dependence in diagnosis must be on roentgen examination, for biopsy is dangerous. It weakens the bone and may cause metastasis

and moreover the histological pictures are not always definite.

Surgical treatment has not proved successful. There have been recurrences as long as fifteen to twenty years after operation; in some cases in which resection has appeared to be complete the tumor has caused metastases and death within a few months. Even in so-called successful cases the bone is greatly weakened and it takes a very long time for restitution—as long as six years or more.

The best treatment is roentgen therapy. At first the area irradiated shows increased osteolysis but after a month or two the clinical symptoms disappear and roentgenograms show progressive reossification at the site of the tumor. Because of the increased osteolysis the limb must be immobilized until reossification occurs.

Roentgenograms of typical cases are given and reference made to previous articles in which further illustrations are given.—*Audrey G. Morgan.*

Olin, Harry A. Primary malignant neoplasm of the shoulder joint, with report of a case. *Radiology*, April, 1944, *42*, 359–367.

Primary malignant tumors of the joints are rare. The anatomy of the shoulder joint is here described in detail and illustrated in order to explain the origin of the tumor described. The patient was a woman of forty-three who had begun to have acute pain in the right shoulder about eight weeks before examination. Motion was limited and there was tenderness throughout the shoulder with some fullness in the anterior and posterior areas. Before the onset of the pain she had been working very hard nursing a son who was ill. The chief roentgen findings were bone destruction in the glenoid cavity, a hazy joint space and multiple small foci of bone destruction in the head of the humerus. A shoulder girdle amputation was performed. Histopathological examination showed an atypical fibrosarcoma originating either in the synovial membrane of the glenoid cavity or in the endosteum. On examination three months later metastases were found in the left femur, knee, left side of the neck and lungs. She died about fourteen weeks after the operation.

Apparently this was a very malignant type of tumor, as evidenced by its rapid growth. Pathologists have frequently said that this type of tumor is radioresistant. But a patient treated by Collins and Anspach responded remarkably well to irradiation though the symptoms at the time of treatment were of two years' duration. Roentgen treatment was not tried in this case. Photomicrographs of the findings are given.—*Audrey G. Morgan.*

BLOOD AND LYMPH SYSTEM

Shrader, E. Lee, Sante, L. R., and Anderson, W. A. D. Clinicopathological conference [lymphoblastoma of Hodgkin's sarcoma type]. *Radiology*, Sept., 1944, *43*, 293–296.

The subject of this conference was a white woman of twenty-one admitted to hospital February 4, 1943, complaining of abdominal pain which had begun ten days before. At first it involved chiefly the right lower quadrant but later became generalized. When the first roentgen examination was made February 3 the pain was colicky in nature and radiated to the back. On admission to hospital February 4 palpation showed the point of greatest tenderness in the midline between the pubis and umbilicus. There was a vaguely palpable mass about 5 cm. in diameter in the right lower quadrant, not freely movable and fairly tender. Normal peristaltic sounds were heard. There was no inguinal lymphadenopathy.

The roentgenogram, which is reproduced, showed several loops of small intestine enlarged to much more than their normal caliber but uniform in size and with no mucosal markings. The inner border was perfectly smooth and an unbroken column of barium was seen throughout the involved segment. There was no peristalsis in this segment and the barium was forced through by pressure from above. There was no constriction in the involved segment or anywhere distal to it and no "string sign." This picture has been seen in malignant infiltration of the wall of the intestine, especially in lymphosarcoma.

Operation was performed February 15. The cecum, appendix and entire ascending colon were indurated and fixed and the process extended backward on the ileum 24 inches; the bowel wall was indurated in this area. The mesentery was thick and contained large nodes.

Enterocolostomy was performed and after a stormy postoperative course the patient died on March 24.

Autopsy showed lymphoblastoma of the Hodgkin's sarcoma type, involving chiefly the small intestine, appendix, spleen and abdominal

pelvic lymph nodes. There was a lesser involvement of the kidneys, adrenals, pancreas, bone marrow, ureters, uterus, fallopian tubes and ovaries.—*Audrey G. Morgan.*

Baker, E. C., and Miller, F. A. Further experiences with venography. *Radiology*, Aug., 1944, *43*, 129–134.

The authors discuss their results in 350 cases of venography. They inject 20 cc. of diodrast into any accessible vein below the ankle through a 25 or 26 gauge needle. The skin is punctured without incision and the dye injected over a period of two minutes. Three 14×17 inch films are used, with two exposures to a film, using half of the film for each. The paired exposures are made from stereo positions. Two cover the area from the ankle to the knee, two the area of the upper leg, knee and lower thigh and two the remainder of the thigh and the lower pelvis. These exposures give three overlapping pairs of films covering the area from the ankle to the lower pelvis. In normal and most abnormal subjects there is complete visualization of the venous system of this whole area.

The venographic patterns may be classified into those of acute and chronic block of the superficial and deep venous plexuses. Treatment of a block of the superficial plexus does not require such radical measures as one of the deep plexus. Three types of venous thrombosis that have been observed are described and four methods of abnormal venous return from the thigh to the body demonstrated. These types are illustrated by venograms.—*Audrey G. Morgan.*

Erf, Lowell A., and Jones, Harold W. Radio-phosphorus—an agent for the satisfactory treatment of polycythemia and its associated manifestations; report of a case of polycythemia secondary possibly to Banti's syndrome. *Ann. Int. Med.*, Oct., 1943, *19*, 587–601.

Eleven patients were studied, 6 were white males, 4 were white females, and 1 was a colored female. These patients had had polycythemia from two to eight years or more before therapy with radioactive phosphorus was instituted. The course of polycythemia varies markedly. All had received many types of therapy previous to radiophosphorus, such as roentgen irradiation, ultraviolet irradiation to the skin and to autotransfused blood, Fowler's solution, phenylhydrazine, venesection, etc., but none had had satisfactory remission following such treatment.

All of the radioactive phosphorus solutions were injected intravenously. The majority of the total dosages varied between 7 and 11 millicuries. Since the average life span of the human red cell is approximately sixty to one hundred days, the first significant hematological responses occurred about sixty to one hundred days after the first injection of radiophosphorus.

After treatments with radiophosphorus the patients usually gained weight, developed unusually good appetites and had clinical and hematological remissions. All skin manifestations disappeared completely after treatment with radiophosphorus and have not returned for over one year. In 8 of the 9 cases studied the red blood cells became larger after treatment with radiophosphorus. This was shown by an increase in the mean corpuscular volume. The coagulation time was reduced following therapy. However, 3 patients had gastric hemorrhage following therapy with radiophosphorus. In one of these the bleeding was fatal. In the second case the bleeding followed the injection of iron, and the remission of the polycythemia was brought about by phlebotomy and additional treatment with radiophosphorus. The third case was complicated by the presence of a Banti's syndrome and the gastric hemorrhage was fatal.

The 11 patients reported here, plus 6 reported previously, have stated that the remission following radiophosphorus was satisfactory and that no other therapy had given equally satisfactory remission. It must be brought out that none of these patients had received "spray" roentgen therapy which has been reported to give excellent remissions in polycythemia. The mechanism of these two types of therapy may be similar. Radiophosphorus concentrates in the bone marrow and continuously bombards such tissues for days. Both radiophosphorus and roentgen irradiation probably decrease red blood cell production by retarding mitosis of normal blood in early prophase. Radiophosphorus is not a red blood cell lytic agent as a metylhydrazine because neither jaundice nor increased excretion of urinary urobilinogen has been observed following administration. In both types of treatment, radiophosphorus and "spray" roentgen irradiation,

the period of irradiation of beta particles is prolonged which may be the effective factor.—*J. J. McCort.*

Carpenter, Gurth, Schwartz, Henry, and Walker, A. Earl. Neurogenic polycythemia. *Ann. Int. Med.*, Sept., 1934, *19*, 470–481.

Two cases of polycythemia associated with subtentorial hemangioblastomata are reported. In the first case all the findings present at the time of clinical examination might have been the result of polycythemia. However, the history of marked unsteadiness of gait shortly after the onset of the symptoms suggested a cerebellar lesion. The marked papilledema and intracranial hypertension seemed out of proportion to what might have been expected if the intracranial disease was entirely on the basis of polycythemia. In the second patient there were no clinical findings pointing to the cerebellum. The diagnosis was made by ventriculography. The absence of symptoms was probably due to the location of the tumor in the lateral part of the left cerebellar hemisphere without involving the cerebellar nuclei. Even large tumors in that region fail to produce cerebellar signs. In neither of these patients was there any evidence of dehydration which might in itself give rise to a high erythrocyte count. In both cases a cerebellar hemangioblastoma was found at operation. Following removal of the tumors the polycythemia disappeared.

In the discussion it is pointed out that intracranial lesions are frequent occurrences in polycythemia rubra vera. Previously, the nervous lesion had been regarded invariably as a function of the primary polycythemia. In the past two decades, however, there have been several articles in the literature devoted to the thesis that polycythemia may be due to lesions in the brain substance. For the most part the reports of neurological damage related to polycythemia do not bear critical analysis. Experimental work is reported which supports the possible presence of a center for regulation of the erythrocyte level in the diencephalon.

That the pathological type of tumor may have played an etiological role in the polycythemia does not seem probable in view of the fact that in a series of 14 other cerebellar hemangioblastomas none has had any evidence of erythrocytemia. Although it is well known that hydrocephalus due to fourth ventricle tumors does cause a dysfunction of the hypothalamic centers, it is difficult to understand the mechanism by which such a neoplasm could selectively influence one diencephalic function. And even were that possible, why should the tumors in the 2 cases reported have produced such selective alterations and other tumors similarly situated and with equally severe hydrocephalus have failed to do so? These considerations make it difficult to assert a diencephalic origin of the polycythemia.—*J. J. McCort.*

GENERAL

Piqué, José A., and Boveri, Juan C. Esfacelo de piel por hematoma migrador y disecante postoperatorio. (Gangrene of the skin from migratory and dissecting postoperative hematoma.) *Rev. ortop. y traumatol.*, April, 1943, *12*, 363–370.

A case is described and illustrated with photographs and roentgenograms. The patient was a woman of fifty-four who had had an intra- and extra-articular arthrodesis of the ankle performed under spinal novocain anesthesia for a bimalleolar fracture following which vicious consolidation had taken place. A large hematoma developed which migrated by dissection to the upper third of the thigh where it produced gangrene of the soft parts in some areas.

The possibility of a postanesthetic nervous complication was excluded and it appeared evident that the hematoma was brought about by vascular changes. The spontaneous hemostasis which occurs in normal patients had not taken place in this patient because of the generalized arteriosclerosis with which she was affected which had prevented rapid contraction of the muscle tunic and retraction of the elastica of the sectioned arteries. As a result of this a much more copious hemorrhage had taken place than is usual in this kind of operation and in the first few hours blood flowed from the wound and filled the cast. The hematoma drained through the subcutaneous tissue of the anterior part of the foot and, favored by the position of the limb, migrated to the root of the thigh. On reaching the lower insertion of the patellar tendon it ran around the lateral surface of the patella and finding a plane of cleavage produced a true dissection of the skin which led to gangrene. It continued upward to the boundary between the middle and upper thirds of the thigh, causing hemorrhagic phlyctenulae and circumscribed areas of gangrene; here it

was stopped by evacuating punctures. Early evacuating punctures should be used in such cases.—*Audrey G. Morgan.*

Pascucci, Lucien M. Roentgen detection in an Army General Hospital of chronic diseases not excluded by induction boards. *Radiology*, April, 1944, *42*, 375–379.

The author concludes from his experience in the O'Reilly General Hospital, a 2,200 bed institution serving the entire 7th Army Command, that many cases of chronic disease are passed over without detection by induction boards, and men admitted who are not fit for military service. The conditions most likely to be overlooked are bronchiectasis, urinary calculi, post-traumatic brain atrophy, herniated disk, spondylolisthesis, colitis and ulcer of the stomach and duodenum. Often the men do not mention their symptoms either because they are not questioned specifically about them or because they do not consider them serious. Medical boards often do not have time to take the careful histories that should be taken and special roentgenologic procedures such as bronchography, intravenous urography, encephalography, myelography, gastrointestinal series and barium enema studies are not carried out. As a result many recruits are admitted with the above-named diseases and possibly others, who are not really fit soldier material. The author's statistics show that 71 per cent of the patients with these diseases had them before induction and that their average length of time in the service was eight months. This is obviously not long enough for the development of a trained soldier and much time and money is expended on these men who have to be discharged back into civilian life.

The more careful taking of histories and more adequate roentgen examinations by trained personnel are recommended as a means of avoiding this waste.—*Audrey G. Morgan.*